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NATURAL FOCALIZATION AND THE EPIDEMIOLOGY OF THE PARTICULARLY DANGEROUS INFECTIOUS DISEASES.

[Following is a translation of selected chapters of a book entitled Prirodnaya Ochagovost' i Epidemiologiya Osobo Opasnykh Infektsionnykh Zabolevaniy (English version above), Saratov, 1959, pp 5-17; 40-53; 54-64; 65-84; 85-96; 100-113; 114-116; 181-187; 337-344; 345-347; 348-355; 356-360; 361-366; 367-371; 437-451; 502-513; 545-551; 552-558; 559-563.]

Table of Contents

pp 9-17

Epizootic Status of Natural Foci of Plague in the USSR in 1954-1956 and an Analysis of the Measures Taken

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Natural Foci of Plague

In the USSR, as is well known, there are active natural foci of plague which occupy extensive spaces on the territory of Kazakhstan, in Central Asia, the lower Volga region, the Transcaucasus and Transbaikal.

The fruitful study of Academician Ye. N. Pavloskiy on diseases with natural focalization based on plague investigations by Russian and Soviet scientists D. K. Zabolotniy, N. A. Gayskiy, N. F. Gamaleya, D. A. Gayskiy, I. A. Deminskiy, I. G. Ioff, N. I. Kalabukhov., N. N. Klodnitskiy, S. N. Nikanorov, P. N. Stupnitskiy, I. S. Tinker, M. M. Tikhomirova, V. N. Fedorov, B. K. Fenyuk, and many others, afforded the basis for determining the existence of the following natural foci of plague on the territory of the USSR: 1) Caspian; 2) Central Asiatic, which is divisible into plain and mountainous portions; 3) Transcaucasian, and 4) Transbaikalian.

During the course of studying plague more than 40 species of rodents and an even larger number of species of fleas were demonstrated which maintain the focalization of plague. Undoubtedly, not all these rodents and fleas are of the same significance in plague focalization.

The Caspian focus includes the Caspian lowlands. The northwestern boundary of the focus basically passes through the Yergeni heights and the Manych semidesert, including the lowland regions lying to the North (Groznyy) and East (South of the mouth of the Sulak River) to the eastern boundary of the Caucasus. To the North, on the right bank of the Volga the focus extends to the bend of the Volga River in the region of Stalingrad, and in the area between the Volga and Ural Rivers, to the mouth of the Kushum River. In the East the focus goes across the Ural River and includes Dzhamboybinskiy, Karatyubinskiy, Taypakskiy rayons of Zapadno-Kazakhstanskaya Oblast and Kzyl-Kuginskiy Rayon of Gur'yevskaya Oblast, joining up with the Central Asiatic focus in the [illegible]thern portion of the Transurals, whereby the boundaries [illegible] them are indistinct.

In the steppe portion of this focus the main vector and reservoir of the plague infection is the population of

dwarf sousliks (Citellus pygmaeus Pall.), from which in the summertime, as the result of contact with them, cases can occur among people. In the sandy portion of the focus the main vectors of plague infection are the meridional jird (Meriones meridianus Pall.) and possibly the crested jird (M. tamariscinus Pall.).

In the autumn-winter, house mice [Mus musculus] and small voles which are infected by plague from sousliks and jirds even in the summertime can participate in transmission of the infection to man.

The Central Asiatic focus is the most extensive of Soviet foci. It extends from the eastern shore of the Caspian Sea in the West to the mountain ranges of eastern Tyan'-Shan' and Tarbagatay in the East. Its northern boundary passes approximately along the Priembinskiy Plain, north shore of the Aral Sea and southern part of the Kazakhskiy melkosopochnik [Kazakh hills]. The southern boundary goes beyond the limits of the Soviet Union, to Iran, Afghanistan and China. In the Southwest the focus joins up with the Iran-Asia Minor and Transcaucasian foci; in the Northwest, with the Caspian focus.

Studies of recent years, made in the Central Asiatic focus, give us quite a complete and specific idea about it. The main vectors and reservoirs of plague infection in the plain (or desert) region of this focus are the great sand rats (Rhombomys opimus Licht.), which, together with other rodents, serve as the source of plague in people. An essential part in the distribution of the plague pathogen in this focus is played by red-tailed jirds (Meriones erythrourus Gray).

In the mountainous portion of the Central Asiatic focus the plague reservoirs are the Altai marmots (Marmota baibacina Katsch) and long-tailed marmots (M. caudata Geoffr.).

The Transcaucasian focus is bounded on the North by Bol'shoy Kavkazskiy Khrebet [Great Caucasian Range], while its southern boundary passes beyond the limits of the Soviet Union into Turkey and Iran. To the West the focus extends to the middle course of the Kura River (region of Rustava) and to the East, to the Caspian Sea.

On the territory of the Transcaucasian focus the main role in maintaining the plague enzootic is played by jirds, possibly including the red-tailed jirds.

The Transbaikalian focus is part of the extensive Central Asiatic focus. Its southern part borders on plague-enzootic areas of the Mongolian People's Republic. The western boundary of the focus passes along the Argun' River (near the village of Sredne-Argunskiy). The northern boundary coincides with the area of desert steppes. To the East the

focus extends to Lake Borun-Torey. The main vector and reservoir of plague in this focus is the tarbagan (Marmota sibirica Raddo).

A significant factor in the spread of plague has been camels, which were infected from rodents and their fleas, because cases of plague in camels were observed only in places of active epizootics among rodents. Infection of people from sick camels occurred from quartering them, removing their hair and dressing the carcasses.

In the USSR there are no permanent rat foci of plague. Brief epizootics of plague among rats observed in Russia which served as the cause of infection of people (in Odessa in 1901, 1902, 1910 and in Batumi in 1901, 1916 and 1921) were the results of importation of plague infection into these ports from without.

An exceptional role in the rooting of plague, in its spread and transmission to man is played, as is well known, by rodent ectoparasites and, chiefly, fleas. We cannot overlook the extensive investigations of this subject in the USSR made by Soviet parasitologists under the supervision of Professor I. G. Ioff. The combination of fundamental investigations of the significance of various species of fleas in natural foci of plague made by I. G. Ioff made it possible to work out a number of new concepts which have obtained broad recognition.

The Epizootic Status of Natural Foci in 1954-1956

While in the past, at the end of the 19th century and the first quarter of the 20th century, in the area of the natural focalization of plague plague epidemics among the local population were observed which in various years took scores and hundreds of human lives, since approximately 1928, since the time of extensive development of measures against plague, cases of plague among people in the USSR are practically not encountered.

At the same time, plague epizootics among rodents observed in past years continue to occur even now in a number of regions of the area of natural plague foci. In certain years, the epizootics included considerable territory and occurred in acute and diffuse forms.

Before proceeding with the characterization of the 1954-1956 epizootics we should present certain data on the census and distribution of the most important rodents and fleas in Soviet foci.

The Caspian focus. In the northwest Caspian, in its steppe portion, the census of sousliks and their fleas remained more or less stable throughout 1954-1956 and was

relatively low. A somewhat increased souslik census was noted in Dagestanskaya ASSR, Astrakhanskaya Oblast and in the southern rayons of Stalingradskaya Oblast.

In the sandy portion of this focus--the Volga-Ural sands--both species of jirds and their fleas did not show any marked increase in census, by and large, in these areas, although in a number of rayons of Gur'yevskaya Oblast, beginning with 1955, a certain increase was observed in the number of jirds and their fleas.

Central Asiatic Focus. In the plain portion of this focus the census of jirds, [here and there it is a little awkward to express the content of the word used here, because the noun "peschanka" means "great sand rat" when used with one adjective and means "jirds" when used with other adjectives; as a matter of fact, these animals are generally known as "sand rats"; the term "gerbil" is also applied loosely here; actually, jirds are gerbils belonging to genus Meriones], including the great sand rats and red-tailed jirds and their fleas, markedly decreased in 1954-1956; however, on the territory of Kara-Kalpakskaya ASSR and Kzyl-Ordinskaya Oblast of KazakhSSR the census of jirds and great sand rats and their fleas remained high. In 1956, in certain places of the Krasnovodskiy plateau, in the southern rayons of TurkmenSSR, as well as in Zhilokosinskiy and Makatskiy rayons of Gur'yevskaya Oblast a local increase in the census of great sand rats was noted.

In the mountainous part of the Central Asiatic focus, chiefly in KirgizSSR, the marmot census was high and remained almost stable during those years. The census of marmot fleas was low.

Transcaucasian Focus. On the Apsheron peninsula, where in 1953 there was mass multiplication of red-tailed jirds, the census of these jirds and their fleas was markedly reduced in 1954-1956. An increased census of jirds and their fleas was observed only in the steppe northwestern rayons of AzerbSSR.

In the Transbaikalian focus the census of marmots and their fleas was low. A reduction of the census of marmots in this focus occurring every year should be noted.

All the data on the census registration of rodents and their fleas give us basis for believing that with the exception of the regions indicated above it was low everywhere in 1954-1956, which had an indubitable influence to varying degrees on the epizootic processes in natural foci.

In the last three years in all the foci 2,643 cultures of the plague microbe were isolated from rodents and their ectoparasites: from sousliks, six cultures; from marmots, 86; from great sand rats and jirds, 975; from other rodents, 10; and from fleas and other rodent ectoparasites, 1,566

cultures. From these, in 1954, 1,532 cultures were isolated; in 1955, 719, and in 1956 (up to 1 November), 392 cultures.

I shall present the figures for isolation of plague cultures for the separate foci.

In the Caspian focus in three years only five plague microbe cultures were isolated. Two of these cultures were obtained on the territory of Astrakhanskaya Oblast, including one culture which was isolated in April 1954 from a group of jerboas (Scirtopoda telum Licht.) caught in the Volga region, and another in 1955 from a dead souslik found in Kharabalinskiy Rayon on the border of Gur'yevskaya Oblast. The other three cultures were obtained in Kizilyurtovskiy Rayon of Dagestanskaya ASSR in May 1956; of these, two were from the bodies of sousliks and one, from fleas taken from souslik holes.

In other years, in Astrakhanskaya Oblast and Dagestanskaya ASSR, just as in the other oblasts of the Caspian focus no epizootics were found in the entire period.

In the Central Asiatic focus during these three years 2,438 cultures of a plague micribe were isolated. I shall give the characteristics of the epizootic status of Central Asia by individual republics and oblasts.

In TurkmenSSR active diffuse epizootics occurring among great sand rats and jirds, which began in 1953, chiefly among the red-tailed jirds, continued during 1954-1955 on the territory of Krasnovodskaya and Ashkhabadskaya oblasts. During these two years 1,279 cultures of the plague pathogen were isolated from rodents and their ectoparasites from 194 "points", whereby about 1,000 cultures were obtained from fleas caught in the holes of great sand rats and jirds. In addition, in 1955-1956 three cultures of the plague pathogen were isolated in Tashauzkaya Oblast; of these, one culture was obtained from a great sand rat in 1955 caught 110 kilometers to the southwest of the city of Tashauz; two cultures in 1956 were taken from fleas which were obtained from great sand rat holes in Takhtinskiy Rayon. In Krasnovodskaya and Ashkhabadskaya oblasts in 1956 it was impossible to find plague among the rodents.

In UzbekSSR in 1954-1955 108 plague microbe cultures were isolated from red-tailed and meridional jirds and their fleas from 24 "points" of Tamdinskiy Rayon of Bukharskaya Oblast. In 1956, in this area no cultures were isolated.

In addition, in Uzbekistan in three years 270 cultures were isolated on the territory of Kara-Kalpakskaya ASSR from great sand rats and meridional jirds and their fleas. Thereby, 70 cultures were isolated in 1954; 138, in 1955 from rodents caught in the environs of the village of Kipchak along the edge of the Kyzyl-Kumy sands, and 62 cultures in

1956 in the northeastern part of Takhta-Kupyrskiy Rayon.

On the territory of KazakhSSR, in the part of it which lies within the limits of the Central Asiatic focus, during this period of time 568 cultures of the plague pathogen were isolated at the following places:

In Gur'yevskaya Oblast (the Priembinskiy Plain and Mangyshlak) 255 cultures were isolated in three years. Of these, 16 cultures were obtained in 1954 from great sand rats, from the dwarf souslik and their fleas in Zhilokosinskiy Rayon and two cultures in the south of Mangyshlak.

In 1955, an epizootic in Mangyshlak occurred in an active form, and on the teritory of Shevchenkovskiy and Mangistausskiy rayons 150 cultures were isolated from great sand rats and red-tailed jirds and their fleas.

In the spring of 1956 the epizootic in Mangistausskiy Rayon continued, and in the autumn an exceptionally active epizootic of plague was demonstrated among great sand rats in Zhilokosinskiy and Makatskiy rayons, which included an oil industrial region and a railroad line almost from the city of Gur'yev to Dossor station. In all, in 1956 86 cultures of the plague pathogen were isolated.

In Kzyl-Ordinskaya Oblast severe epizootics among great sand rats were recorded in the last three years along the line of the Orenburg Railroad, whereby in 1954 an epizootic was recorded also to the northeast of the city of Aral'sk and on the left bank of the Syr-Dar' River. In all in this year 96 cultures of the plague microbe were isolated from 28 "points". In 1955 the epizootic was found on the territory of Aral'sk, Karmanchinskiy and Kazalinskiy rayons, where 165 cultures of the plague pathogen were isolated from the great sand rats and meridional jirds and their fleas at 38 "points". In 1956, along the Baykhozhinskaya and Karakumskaya highways and to the east of the city of Aral'sk 43 cultures were isolated from 20 "points".

In characterizing the epizootic in Kzyl-Ordinskaya Oblast it should be noted that in 1954-1955 the epizootic extended to the southwestern portion of Karagandinskaya Oblast on the border of Kzyl-Ordinskaya Oblast, where from 5 "points" 19 plague microbe cultures were isolated from great sand rats. Until this time plague epizootics had never been recorded in Karagandinskaya Oblast.

In Taldy-Kurganskaya Oblast (Sary-Ishik-Otrau Sands), where plague epizooticshad not been observed since 1950, five cultures were isolated in the summer and autumn of 1956 on the territory of Karatamskiy Rayon, including four cultures from great sand rats and one from fleas.

Finally, in Alma-Atinskaya Oblast an epizootic was found on the territory of Narynkol'skiy Rayon, where in 1955

and 1956 four cultures of the plague pathogen were isolated from marmots and their fleas.

In KirgizSSR in the three years 263 cultures of plague microbe were isolated from marmots and their ectoparasites in Issyk-Kul'skaya and Tyan'-Shan'skaya oblasts (the region of Novo-Voznesenskiy, Pokrovskiy and Dzhety-Oguzskiy syrts [quicksands] and Vostochniy Aksay Valley). Thereby, the majority of these cultures, amounting to 166, was isolated in 1956.

Within the limits of the Transcaucasian focus in 1954 no epizootics were recorded. In 1955-1956 150 cultures of the plague pathogen were isolated on the territory of AzerbSSR, where in 1953 an active epizootic was found in red-tailed jirds including the entire Apsheron peninsula and regions located to the north of Baku. Thereby, in 1955 the plague epizootic included the central and northwestern portions of Azerbaydzhan--Yevlakhskiy, Safaraliyevskiy, Kusum-Izmaylovskiy, Tauzskiy, Agdzhabedinskiy rayons and came close to the boundary of Georgia. In all, in 1955 127 cultures of the plague pathogen were isolated. In 1956, the cultures of the plague microbe were isolated in the same areas as well as in Shamkhorskiy Rayon. Twenty-three cultures were isolated, chiefly from fleas and ticks of the red-tailed jirds.

The Transbaikalian focus, in contrast to the other natural foci, is in a burned-out state. From 1947 through 1956, despite careful investigation, not a single culture of the plague microbe was isolated in the Transbaikal.

Analyzing the epizootic processes which occurred in 1954-1956 on the territory of all the natural foci it may be said that by comparison with the period before 1954 a smaller territory was included by the plague epizootics, and they as a whole showed a tendency toward decreasing. This also had an influence on the progressive reduction in the total number of plague microbe cultures isolated in natural foci of the USSR every year in the period from 1954 through 1956 (see above).

In 1954, the plague epizootics were still occurring actively, although in this year by comparison with 1953 a decrease in the epizootic activity was noted in a number of places. An active epizootic was found in 1954 in the Central Asiatic focus in the territories of the TurkmenSSR, UzbekSSR (including Kara-Kalpakskaya ASSR) and Kzyl-Ordinskaya Oblast of KazakhSSR.

In 1955, the number of places in which active epizootics were found decreased even further, although on the territories of the Central Asiatic, Transbaikalian and partly in the [illegible] foci (Kzyl-Ordinskaya and Gur'yevskaya Oblasts of [illegible]khSSR, UzbekSSR together with Kara-Kalpakskaya ASSR and [illegible]bSSR) the plague epizootics continued to occur quite acutely and encompass relatively large territories in places.

Finally, in 1956 the activity of the natural plague foci decreased sharply, which was expressed in a particularly

clear-out manner in West Turkmenia, in the central, southern and northern parts of Kyzyl-Kumy. In Kara-Kalpakskaya ASSR and Kzyl-Ordinskaya and Gur'yevskaya Oblasts of KazakhSSR local acute epizootics of plague continued.

In contrast to what has been stated, in the mountainous regions of the Central Asiatic focus the plague epizootic had quite an active course during all the three years among the marmots. It should be emphasized that in the three years being described the epizootics were found in new places, where they had never been recorded before, namely: in 1956, on the steppe areas of the middle portion of Kurinskaya Plain in Azerbaydzhan; in 1954-1955, in the southwestern part of Karagandinskaya Oblast, and in 1956, in new places on the territory of Dagestanskaya ASSR.

An evaluation of the course of plague epizootics in past years with consideration of the census of rodents and fleas in 1956 and the suspected census of them in 1957 under the specific conditions of various natural foci permits us to suppose that in 1957 it is possible to expect a certain increase in the epizootic activity of plague in a number of the foci. This obliges us to increase investigative and prophylactic work in the foci.

In the Caspian focus chiefly the territory of Astrakhanskaya Oblast, the eastern part of Groznonskaya Oblast, the northeastern part of Stavropol'skiy Kray and the lowland portion of Dagestanskaya ASSR deserve concentrated attention; here, the probability has not been ruled out of occurrence of local plague epizootics among sousliks. On the left bank of the Volga, specifically in the Volga-Ural sands, the occurrence of local epizootics among great sand rats and jirds is possible.

In the Central Asiatic focus the territory of Gur'yevskaya and Kzyl-Ordinskaya oblasts and Kara-Kalpakskaya ASSR deserves special attention; here, plague epizootics can encompass new spaces and proceed in an active form. In TurkmenSSR it is also possible to suspect an increase in the epizootic process. The demonstration of various epizootic "points" in Karagandinskaya, Yuzhnaya-Kazakhstanskaya and Dzhambul'skaya oblasts is entirely possible.

The mountainous portion of the Central Asiatic focus should, as before, be in the center of our attention, because epizootics of plague among the marmots will apparently occur in an active form in 1957 also.

In the Transcaucasian focus the steppe regions of AzerbSSR deserve special attention, because plague epizootics among great sand rats and jirds will possibly increase and can encompass new territory; the possibility has not been ruled out of the penetration of the epizootic into the terri-

tory of GeorgSSR and the renewal of it in the Apsheron peninsula.

In the Transbaikalian focus there is no reason to expect the occurrence of a plague epizootic.

Organizational Structure and Arrangement of the System of Plague Institutions.

The organizational structure and arrangement of the system of plague institutions has been constructed based on the epidemic and epizootic situation which has been built up with regard to plague in the USSR and in adjacent countries. Long years of experience in the organization and in the existence of the plague system as a single centralized system has shown the full advantages of it. Such a centralization has contributed to complete and timely fulfillment of the main task confronting the plague system, that of providing epidemic welfare in the country with regard to plague. The existing structural principles of the plague system have made it possible to take all measures for prophylaxis and control of plague without regard to administrative boundaries of republics, krays or oblasts through the personnel and facilities of the entire system of plague institutions.

In accordance with this, in 1954-1956 the territories accommodated by the plague institutes and stations were revised; new plague stations and departments were organized. At the same time, part of the plague institutions was eliminated or reorganized.

At the present time, the system of plague institutions includes five plague scientific research institutes, eighteen plague stations (with 72 departments), five port plague laboratories and two city and port plague observation stations.

Sanitary-Prophylactic and Antiepidemic Plague Measures

The systematic and timely accomplishment of a combination of sanitary-prophylactic measures has played a tremendous part in assuring epidemic welfare with regard to plague. In the investigative work, aside from permanent plague institutions, 528 provisional epidemiological detachments were included; of these, 181 were started in 1954; 182, in 1955; 165 detachments, in 1956. The new tactics of epidemiological reconnaissance developed by the plague institutes made it possible to investigate more extensive territories by comparison with the previous period.

By epizootological investigation, that is by systematic observation of the status and census of rodents and their fleas and investigation of them for plague infection almost

all territories with active and threatened plague were included in 1954-1956. Every year, up to 40,000,000 hectares of field area as well as a number of ports and large inhabitated places are included in this investigation.

In 1954-1956 more than 2,000,000 rodents and about 10,000,000 ectoparasites were subjected to bacteriological examination. In this very important work a new method of epizootological investigation was used on a large scale, making it possible not only to include large territories but also to determine their epizootic status with regard to plague in a short period of time. This was achieved by means of a differentiated approach to the investigation of one territory or another in accordance with the problems confronting the investigators: in some cases extensive use was made of investigation chiefly of ectoparasites; in other cases, combined investigation of both rodents and ectoparasites.

The investigation made in these years afforded the possibility of timely detection of certain characteristics of the course of the epizootic process, which facilitated the better planning and accomplishment of prophylactic plague measures.

In taking the sanitary-prophylactic measures for the current period the plague institutions gave serious attention to systematic observation of the state of health of the population in regions enzootic for plague. This work was done not only by workers of plague institutions, but workers of the general medical system were also brought in for it, without whom, undoubtedly, it would have been impossible to carry out the medical observation completely. Proper performance of this work should have contributed to timely detection of the first cases of plague in the population if there were any as well as excluding cases occurring from contact and exportation of the infection beyond the limits of the focus. In the light of our knowledge about the treatment of plague the proper organization of the observation of the state of health of the population was able to assure the possibility of timely application of specific treatment, if patients had been detected, and, by the same token, reduce the mortality rate in plague.

In accordance with the prophylactic trend of Soviet public health the control of rodents in the area of natural plague foci is regarded as one of the most radical plague measures. At the same time, it is expedient to revise critically the principles of planning extermination work in the future for the purpose of making them more purposeful.

Rodent extermination in the area of natural plague foci during the period of time being reported, as in previous years, was conducted as a planned government measure, and it was

done on a broad scale. In total, in 1954-1956 the efforts made against various types of rodents--the vectors and reservoirs of the plague microbe--were made on 18,332,300 hectares of field area; of these, 12,641,800 hectares were on the territory of the Caspian focus; 4,501,000 hectares on the Central Asiatic focus; 1,027,900 hectares on the Transcaucasian focus; and 161,600 hectares on the Transbaikalian focus.

In the Caspian focus, including the northwest Caspian, the extermination of sousliks was accomplished on 4,657,300 hectares and of various species of great sand rats and jirds, on 7,744,300 hectares. In the Central Asiatic focus the control of different species of great sand rats and jirds was carried out over an area of 4,005,000 hectares, and of marmots, on an area of 491,100 hectares. In the Transbaikalian focus marmots were exterminated on an area of 161,600 hectares. The extermination of mouse-like rodents in all foci was accomplished over an area of 245,100 hectares.

Note should be made of the incorporation of new methods of controlling rodents, developed by Soviet specialists, particularly the extensive application of poisoned baits and expansion of the arsenal of toxins used.

Rodent extermination in the area of natural plague foci was accomplished with different purposes. In the Caspian focus, specifically in its Volga right-bank portion, that is, on the territory of Astrakhanskaya, Rostovskaya, Stalingradskaya and Groznenskaya oblasts, Stavropol'skiy Kray and Dagestanskaya ASSR the extermination operations were accomplished with the aim of eliminating the natural focalization of plague. South of the Volga-Ural sands (within the limits of Gur'yevskaya Oblast and the left-bank portion of Astrakhanskaya Oblast), in Zapadno-Kazakhstanskaya and Chitinskaya oblasts the purpose of the extermination operations was the prevention of the possibility of the development of an epizootic. In the other places, chiefly in the Central Asiatic and Transcaucasian foci, extermination operations were carried out with the aim of suppressing active plague epizootics and creating the so-called "protective zones" for the purpose of lessening the possibility of plague infection of people.

Systematic extermination of rodents contributed to reducing their census, although this was brief and unstable for certain species of rodents (for example, great sand rats and jirds), and, by the same token, led to a reduction in the infectiveness of the foci. There is no doubt of the fact that through the operations on rodent extermination alone a radical improvement of the situation was achieved in the northwestern portion of the Caspian natural focus, and complete elimination of a plague epizootic over a considerable

portion of it (Stalingradskaya and Rostovskaya oblasts, Stavropol'skiy Kray in 1945). In the southern zone of the Volga-Ural sands repeated extermination of great sand rats and jirds over large territories in recent years made it possible to achieve a satisfactory antiepidemic effect. In the Transbaikalian focus the operations conducted made it possible markedly to reduce the marmot census and improve the focus radically. The problem of finding simpler and more economical forms of keeping the marmot census at a low level in the Transbaikal confronts the plague organization of Siberia and the Far East.

We should point particularly to the broad experience of the AzerbSSR in simultaneous destruction of red-tailed jirds and their fleas by means of using fused cyanides in a mixture with hexachlorane. As the result of these operations a rapid and relatively stable suppression of the epizootic was achieved.

Along with operations on the extermination of rodents under field conditions plague institutions have methodically carried out operations on deratization, insect elimination and disinfection of inhabited places on a large scale. However, these operations were not always conducted with consideration of the epizootological and epidemiological necessity. In 1954-1956 deratization was conducted in a volume of 63,805,600 square meters; insect elimination and disinfection, in a volume of 14,282,300 square meters.

In the general system of prophylactic measures considerable attention has been given to vaccination and revaccination of the population. This measure was taken chiefly for epidemiological indications and was concentrated in areas enzootic for plague. Practice has shown that the percutaneous method of vaccination is most acceptable. Despite the fact that the intradermal method of vaccination gives the greatest and most stable immunity according to experimental data, its use on a broad scale proved to be impractical in connection with the considerable frequency of side-effects of the vaccine after the intradermal method of administering it and the difficulty of organizing large-scale vaccination of the population by this method. In 1954-1956 2,013,100 persons were inoculated with living bivalent plague vaccine.

Scientific Research Work

Along with the practical activity scientific research work has been extensively developed in Soviet plague institutes and stations during this period of time. Scientific research work in the plague institutes and stations was directed chiefly at solving problems associated with the

suppression and elimination of the natural plague foci in 1954-1956. The scientific topics in epidemiology, microbiology, zoology, and parasitology were subordinated to this main problem. In 1956, of a total number of 258 topics the plague institutes worked out 169 and the peripheral plague institutions, 89 topics.

Study of the focalization of infectious diseases in the light of general biological generalizations and the theory of Academician Ye. N. Pavloskiy concerning the natural focalization of arthropod-borne diseases has found its reflection in the scientific research work of Soviet plague institutions. In turn, this in large measure has contributed to uncovering the rules and regulations of plague movement in the natural foci and elimination of this infection.

I consider it necessary to note a number of works accomplished by plague institutions in the past three years which are of great practical importance. As the result of a three-year expeditionary operation a study was made of the basic factors in the natural focalization of plague in Turkmenia. Specifically, the mechanism of transmission of the epizootic from season to season under the conditions of Turkmenia was studied; the epizootological and epidemiological roles of the great sand rats and red-tailed jirds were defined; certain specific characteristics of the effect of fleas on the epizootic process and the possibility of infection of people were detected.

Major expeditionary investigations were made on the study of the mechanism of infection of camels with plague and a search for prophylactic agents against plague in them. As the result of the work done, together with a number of experiments on infection of camels with plague by different methods, it was possible even in 1955 to determine the advisability of inoculating camels with living plague vaccine.

A study was made of new forms and tactics of investigating territories enzootic for plague. The material of this work constituted the basis for revising existing methodological principles of investigation and made it possible to proceed in practice to new forms of investigative work.

In an extensive experiment a study was made of the problems of treatment and emergency prophylaxis of plague. As the result of this work an efficient system was proposed for using the most effective preparations; the advantage was shown of using streptomycin and other antibiotics over therapy with sulfonamides; the mechanism of action of antibiotics was clarified. The work done made it possible to work out instructions for the treatment of plague, which have already been used in practice in antiepidemic work.

An important measure for the prophylaxis of plague was

developed by means of simultaneous effects on both the reservoirs of the plague microbe, rodents, and its vectors, fleas.

The possibility of application of this method under industrial conditions was proved by the work done; this makes it possible to recommend it for practical application as a method which makes it possible in a short time to render the area of a fresh epizootic innocuous. This method also opens up prospects for more rapid improvement of natural foci and definitive elimination of a plague enzootic in them. However, it should be emphasized that the problem of a marked increase in the productivity of work of simultaneous extermination of rodents and their ectoparasites confronts the plague organization.

A number of methods have been improved for controlling rodents and chiefly the method of poisoned baits as applied to sousliks and various types of great sand rats and jirds. Improvements in the gas method of controlling marmots has made it possible to develop considerably more extensive extermination measures for these plague vectors in the mountainous regions of Central Asia and in the Transbaikal than was possible previously.

Time does not permit a more detailed discussion of the volume and results of scientific research work done by plague institutions. A large number of the scientific topics on improvement of diagnostic methods for plague, on the study of the biology and ecology of vectors and reservoirs of the infection and others were subordinated to the main problem, study of the natural foci of plague.

The Problems Next in Turn.

From the materials presented above it is clear that the plague system has made definite achievements both in organizational-practical activity and in scientific research work. However, even greater problems, associated with the further improvement of the natural foci, confront the plague organization.

First of all, it is necessary to develop tactics and methods of suppressing the activity of each natural plague focus separately, and in some cases also complete elimination of this focus on the basis of studying its structure and rules and regulations of the course of epizootics in accordance with the landscape characteristics of its territories.

Closely connected with the solution of this problem is extensive epizootological investigation of all natural foci. In the Caspian focus the right-bank and left-bank portions

of Astrakhanskaya Oblast, Gur'yevskaya Oblast, Zapadno-Kazakhstanskaya Oblast (chiefly the rayons bounding Gur'yevskaya and Astrakhanskaya oblasts) should be included in the investigation. In Stavropol'skiy Kray, Groznonskaya Oblast and Dagestanskaya ASSR the entire steppe area, chiefly the Black Earth and Nogaysk steppes, should be investigated.

In the Central Asiatic focus the main attention should be given to the investigation of the southeastern portion of Gur'yevskaya Oblast, southeastern Kara Kumy, the central portion of western Kyzyl-Kumy, Bukharskaya, Khorezmskaya, Kashka-Dar'inskaya and Surkhan-Dar'inskaya oblasts, the rayons of the Northeastern Urals, Golodnaya Step', Muyun-Kumy sands and Sary-Ishik-Otrau--in the plain portion of the focus--and Alma-Atinskaya oblast, KirgizSSR and TadzhikSSR, in its mountainous part.

In the Transcaucasian focus the Apsheron peninsula and the steppe (or plain) regions of AzerbSSR reaching to GeorgSSR should be investigated. In GeorgSSR and ArmSSR mainly an investigation should be made of the regions bounding AzerbSSR and Turkey and Iran.

In the Transbaikalian focus methodical observations should be established of the entire focus; the regions bounding the Mongolian People's Republic should be examined more carefully.

In the organization of the investigation of ArmSSR, GeorgSSR, TurkmenSSR, TadzhikSSR, KazakhSSR, Buryat-Mongol'skaya ASSR and Tuvinskaya Oblast consideration should be given to the possibility of importation of plague from adjacent countries which have natural foci of this disease, specifically, from Iran, Turkey, the Mongolian People's Republic, and the Chinese People's Republic.

A second important problem is the continuation of operations on the perfection of the methods of controlling various species of rodents. It is necessary to develop effective methods for application of poisoned baits in controlling all the main species of rodents and particularly to solve the problem of the suitability of the bait method of exterminating the dwarf souslik in the southern zone of its area of distribution.

The basis of the determination of the areas on which extermination of rodents and ectoparasites should be accomplished in a planned manner, should be epizootological substantiation with consideration of possible and already posed problems on the complete elimination and radical improvement of natural foci in which this is possible.

A method should be worked out for making predictions of the possible occurrence of epizootics among rodents in order to avoid the unexpected happenings such as occurred in 1954-

1956 in a number of foci.

We do not have at our disposal complete data for the characterization of Soviet natural plague foci. The characteristics of various foci have not yet been adequately studied by plague institutions. This has in some cases led to "unexpected" occurrences of epizootic complications.

On the territory under supervision by the Turkmen, Guryevskaya, Azerbaydzhan and some other plague stations a number of natural factors contributing to increase of the rodent census and that of their ectoparasites preceded the appearance of active epizootics among the ruins; however, these factors and even the mass spread of rodents were unknown to specialists in the plague institutions mentioned above.

Work on the study of the most effective means and methods of immunizing the population against plague which would satisfy all the requirements of mass vaccination, that is, would give a high degree of immunity with few side effects and would be convenient in an organizational respect, deserve special attention. A search for new vaccine strains with good immunogenicity is also needed.

Aside from the resolution of those topics and problems mentioned above plague organizations should: a) intensify operations on the further testing of the therapeutic effectiveness of antibiotics and chemotherapeutic preparations for the treatment of plague; b) intensify investigations on improving the production of diagnostic, prophylactic and therapeutic bacterials by means of mechanizing all the industrial processes and improving the quality of the preparations produced; c) intensify considerably research on plague microbiology, chiefly on developing the fundamentals and methods of early and accurate diagnosis.

In carrying out practical and scientific research operations on plague of great importance is proper arrangement and the organizational structure of the plague institutions. The plague institutes should revise the arrangement of their plague institutions with consideration of maximum coverage of all the natural plague foci with their activity. Unfortunately, to date this problem has not been completely and properly solved. The problem of combining small departments and laboratories with the main laboratories in the institutes has not been solved either.

In the report light was thrown on the epizootic and epidemic status of the natural plague foci; a brief analysis was given of the measures taken and the main prospects of work outlined for the next few years.

An analysis of all the facts which we know of at present in the light of current knowledge of the natural focalization

of plague permits us to consider approximately the following territories of the USSR enzootic and "potentially enzootic" with regard to plague, requiring special attention on the part of the entire plague system: 1) in the Caspian focus--Astrakhanskaya Oblast, Stavropol'skiy Kray, Groznenskaya Oblast, Dagestanskaya ASSR, Gur'yevskaya Oblast, Zapadno-Kazakhstanskaya Oblast; and the southern regions of Stalingradskaya Oblast; 2) in the Central Asiatic focus--the TurkmenSSR, TadzhikSSR, KirgizSSR, Bukharskaya and Surkhan-Dar'inskaya oblasts and Kara-Kalpakskaya ASSR, UzbekSSR, Alma-Atinskaya, Taldy-Kurganskaya, Kzyl-Ordinskaya, Yuzhnaya-Kazakhstanskaya, Dzhambul'skaya and Aktyubinskaya oblasts and southwest Karagandinskaya Oblast of KazakhSSR; 3) in the Transcaucasian focus--the Apsheron peninsula and all the steppe regions located to the northwest and south of Apsheron and bounding Iran in the AzerbSSR as well as the regions bounding Azerbaydzhan, Turkey and Iran in the ArmSSR and the regions bounding Azerbaydzhan and Turkey in the GeorgSSR; 4) in the Transbaikalian focus-- Chitinskaya Oblast, Tuvinskaya Oblast, and Buryat-Mongol'skaya ASSR.

In conclusion, it should be noted that the plague organizations have every possibility for creating epidemic welfare in the Soviet Union with regard to plague.

pp 40-53

The Problem of the Paleogenosis and History of the Natural Plague Focus in the Northwest Caspian Region

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At the level of the current development of knowledge in the field of geology, paleobiology, biogeography, archeology and some other sciences at the present time a real opportunity has been outlined for working out problems of the occurrence and establishment of the natural foci of many infectious diseases including plague. The very fruitful teaching of the natural focalization of arthropod-borne diseases, the founder of which is Academician Ye. N. Pavloskiy, has contributed to this to a considerable degree. On the basis of this teaching a number of Soviet students of the plague-- I. G. Ioff, N. I. Kalabukhov, N. P. Naumov, Yu. M. Rall', I. S. Tinker, V. N. Fedorov, B. K. Fenyuk and others--worked out the most important theoretical principles dealing with the natural focalization of plague, which also serve as one of the main starting points of our research in the field of the paleogenesis and history of the natural plague focus of the northwest Caspian region.

It is not by chance that in the northern hemisphere the natural foci of plague adapted themselves to the southern zone of the temperate latitudes, not spreading further than 50^{o}-51^{o} north latitude. This fact, as is justifiably noted by B. K. Fenyuk (1944, page 40), "...permits us to suspect the existence of some kind of general geographic rules and regulations of plague focalization", which are absent from the other zones. A definite type of climate and landscape are characteristic of the entire territory, which geographically includes the modern plague foci of the USSR. This is the area of open spaces: desert, semidesert, dry steppes, and mountainous desert steppes, covered chiefly by dwarf xerophytic vegetation.

For the purpose of understanding the causes of the natural focalization of plague this fact is of more than a little importance. Under conditions of the relative dryness of the air and soil processes of putrefaction of organic residues are delayed considerably. The rodents' nests are well preserved sometimes for several years, whereby optimum conditions are created for the activity of ectoparasites in the nest and their longevity is assured. It may be supposed that the plague microbe appeared in the biocoenoses of such

areas of dry land specifically, as they were formed, proceeding probably from a saprophytic to a parasitic state at a definite stage of evolution. However, in spite of the opinion of Yu. M. Rall' (1956), we believe that the evaluation of the corresponding facts in order to gain an idea of the nature of the steppes, desert and semidesert of previous geological eras is very difficult. As I. A. Yefremov (1954) points out, taphonomic data are evidence to the effect that by the totality of excavated remains found in the layers of a single geological period without consideration of the burial conditions of those remains it is impossible to gain any kind of complete idea of the fauna and flora of that period. However, for our purposes we must first of all take into consideration the presence or absence of relatively highly organized animals, which rodents are, in previous eras, because as is noted by I. A. Yefremov, functional anatomy gives us reliable results in the most complexly organized organisms, even if the excavated remnants are incomplete. In addition, a large number of excavated remains of rodents, which are chiefly hole-burrowing animals, are found in the old "mole holes" in situ, whereby they belong to the Quaternary, that is, to relatively recent times, as the result of which the time of burial of the animals' can be judged approximately by the degree of fossilization of their bones.

An abundance of geological and paleontological data show that before the beginning of the Neogene system on the territory of Eurasia there were probably no conditions in existence for the occurrence of plague foci of the steppe and desert types. Discussing the problem of the time of occurrence of the pathogenic (not the saprophytic) form of plague bacillus, Yu. M. Rall' (1956) expresses the entirely probable assumption that it was at the beginning of the Neogene system, when the deserts of Eurasia and Africa began to be formed.

While data are still very sparse for claiming the existence of the original foci of plague in the Miocene epoch, and this is done rather on a purely logical basis, there is quite a bit more reliable information for judging the possibility of existence of plague foci in the Pliocene. We must suppose that in the Pliocene the most favorable conditions for the formation of fauna of the desert type existed in the plains of Central Asia where, as has been pointed out by P. A. Kuznetsov (1948, page 164), "even in the Tertiary the landscape of sandy deserts with their characteristic fauna began to be built up gradually". Further, Kuznetsov explains that the idea of such an ancient origin of the desert fauna in the plains of Central Asia is confirmed by the presence there of a number of endemic species and even genera of mammals

(Spermophilopsis, Paradipus, Eremodipus, and others). Probably, biocoenoses began to be created specifically there; these were composed of parasitic arthropods (fleas, ticks) and the plague microbe in addition to rodents of the desert and semidesert types as permanent components.

Yu. M. Rall' (1956) believes that the initial foci of plague occurred under conditions of the mountain plateaus of Central Asia, first in marmots. With change in the climate the marmots descended to the plains and infected new territories, giving plague to sousliks and great sand rats and jirds. As confirmation of his viewpoint Rall' directs attention to the "marmot" nature of plague in Mongolia and Manchuria even at the present time.

In discussing the problem of the time of occurrence of the pathogenic form of the plague bacillus, Yu. M. Rall' correctly criticizes Gill (1928), who, as is well known, believed that the original reservoir of pulmonary plague was constituted by animals of the Ice Age, whereas the bubonic form of plague could appear only in the period after the Ice Age, at a time when vectors, parasites, became involved in the transmission of the disease with warming up of the climate. (Quoted by C. Nicolle (1937)).

It must be supposed that in the Pliocene the ectoparasites of rodents had already acquired their specialization of being parasites of warm-blooded animals, including rodents. V. N. Beklemishev (1951) writes that the group of ticks has been known since the Devonian period. He believes that the purely parasitic group of arthropods--Metostigmata--particularly ixodial ticks, arose in the earliest periods, possibly in the Permian or Triassic periods, while fleas probably arose in the Cretaceous period. I. G. Ioff (1948), studying marmot fleas, concluded that fleas of the genus Oropsylla, parasitic on Marmota bobac, M. baibacina marmots and others are similar to the American species of Oropsylla. Therefore, the genetic similarity between Eurasian (with the exception of the Central Asiatic) marmots and the American badgers has been confirmed by these data. The connection between the continents of Eurasia and America was definitively broken at the beginning of the Quaternary. Representatives of Oropsylla exist on marmots in both continents. Therefore, before the connection was broken between these two continents, that is, in the Pliocene, the related species of fleas of the genus Oropsylla were already parasitic on marmots.

Returning to the problem of the plague pathogen, it should be noted that V. O. Tauson, for example (1936), considers microbes a very ancient group of organisms, the most diverse forms of which manifested their activity in the earliest periods of life on earth. N. F. Gamaleya (1939) pro-

sents data to the effect that the first pathogenic bacteria were found in osteomyelitis in the Dimetrodon, the geological age of which has been determined at approximately 15,000,000 years. V. M. Zhdanov (1953) points out that "plague and tularemia were created as infections of rodents during the period of existence of broad connections between the continents. The colonizing rodents spread the infection, which since that time has progressed very little--so little in fact that plague and tularemia microbes isolated in different countries are not much different from each other. The differences between them are only those which can indicate different ecological or non-geographic varieties" (page 140).

As far as the South of the European portion of the USSR is concerned, judging by excavated remains of animals and plants, we may suppose that here there were no extensive desert or semidesert landscapes before the period of the Rissian-Wormian interglacial stage. (Many Soviet paleontologists divide the Quaternary into the ancient or early Pleistocene (the Homicene according to Pidoplichko, 1946), the middle Pleistocene, the upper Pleistocene and the Holocene. In the history of the Caspian region they correspond to the Baku, Khazar, Khvalynsk transgressions of the sea and the post-Khvalynsk era. The Rissian-Wormian interglacial stage corresponds to the middle and beginning of the upper Pleistocene). The dry-valley areas of the steppe could occur only on the highest places, possibly in the foothills of the Caucasus and in Yergeni, where they were separated by the forest vegetation, frequently of the ravine type, the excavated remnants of which are known in those areas. Everything presented thus far leads to the conclusion that plague at that time could not have taken root in the biocoenoses of the European part of the USSR.

The paleontological investigations of B. S. Vinogradov (1937), A. I. Argiropulo and A. V. Bogachev (1939), A. A. Argiropulo (1941), N. K. Vereshchagin (1942) and others show that at the end of the Rissian-Wormian stage (the end of the middle and upper Pleistocene), that is, about 80,000-100,000 years ago, many species of rodents characteristic of desert and semidesert areas lived in the Transcaucasus and Crimea. B. S. Vinogradov justifiably points out that the rodent fauna of the Crimea of that time showed a definite similarity to the modern fauna of deserts and semideserts of the region on the left-bank of the Volga.

Probably, at the end of the Rissian-Wormian stage the desert and semidesert group of rodents was widespread, which is evidenced by the areas of distribution of the remains of many species in the Ukraine: the scirtopod jerboa [Scirtopoda telum] ("Aleshkinskiye Peski"), the social vole [Micro-

tus socialis], mole vole [Ellobius talpinus] and others. In the light of what has been stated, N. Sharleman's statement (1935) that the scirtopod jerboa could have penetrated into the Ukraine only in the postglacial period is erroneous in our opinion.

Excavated remains of rodents within the limits of the Volga-Don watershed, found and described by I. M. Gromov (1956, 1956a, 1956b) are particularly interesting. Of the Pleistocene deposits (chiefly, the upper Pleistocene and Holocene) remains of the souslik, similar to the large souslik, remains of the Caspian souslik [Citellus fulvus], dwarf souslik [Citellus pygmaeus], the Aral thick-tailed jerboa, the hairy-footed jerboa [Dipus sagitta], the yellow lemming [Lemmus sp. ?], the scirtopod jerboa, steppe cony [Ochotona sp. ?], and others have been found along the Don and Volga. To this we can add the finding of S. I. Obolenskiy (1927), on the right-bank of the Volga in the vicinity of North Zam'yana, of remnants of the great sand rat.

I. M. Gromov emphasizes that in the second half of the middle Pleistocene the rodent fauna of the Don and Volga steppes was to a considerable degree similar in its composition to the fauna of the left bank of the Volga and West Kazakhstan. Judging by the appearance of the Pleistocene rodent fauna, which to a considerable degree were the inhabitants of dry steppes, semidesert and desert, it is difficult to doubt that the ecological conditions were on hand for inclusion of the plague microbe in the biocoenoses at that time on the territory of the South of the European portion of the USSR, particularly on the territory of the northwest Caspian area. If this is so, then, first of all, primitive man could have been affected by plague; secondly, this ancient focus of plague in Europe was incomparably more extensive than the present-day focus.

The idea that the Caspian focus is the remnant of a more extensive spread of plague in Europe has been stated by V. N. Fedorov (1950). He considers it possible to refer the formation of the European focus of the plague enzootic to a time which preceded us by no less than 100,000 years. The possibility of the existence of a more extensive enzootic focus of plague in Europe in the past has also been assumed by H. Sticker (1908), V. Ye. Zabaluyev (1913), N. N. Klodnitskiy (1925), and I. G. Ioff (1936). Subsequently, for many hundreds of years, this tremendous European focus of plague has undergone definite pulsations under the influence of changes in climate and variations in the seas, to follow which it would be extremely difficult to do at the present time.

At the end of the Pleistocene (about 20,000 years ago) the Caspian basin increased in size, giving rise to the

Khavlynsk Sea. In the stage of its greatest development it flooded all of Astrakhanskaya Oblast and reached Kamyshin in the North; in the West, Yergeni. The Black Sea basin, in turn, expanded considerably, after becoming connected with the Khavlynsk Sea through the Kumo-Manychskiy Proliv [strait]. The area of land to the south decreased in size markedly. There was also a change in the climate--it became generally more humid and warmer. The boundaries of the natural plague focus undoubtedly changed also. Probably, this period was distinguished by a considerable "quiescence" of plague events.

The most recent geological data show that the Khavlynsk transgression ended very quickly, after which came the Mangyshlak regression, as the result of which the Caspian decreased very much in size: its north shore was approximately on the line connecting Makhachkala and Groznyy. About 4,000-5,000 years ago the last so-called "Nikol'sk" transgression of the Caspian occurred, when the seashore, as during the time of the Khavlynsk transgression, was constituted by the Yergeni heights.

After the Nikol'sk transgression the most recent history of the plague focus of the northwest Caspian begins essentially, corresponding to the postglacial period, including the modern era.

Many investigators (Pachoskiy, 1917; Lavrenko, 1938; Berg, 1947 and others) believe that about 3,000-5,000 years ago the climate in southern Europe was dry. L. S. Berg believes that during this xerothermic period the Kherson steppes were a desert similar to the present-day right-bank area of Astrakhanskaya Oblast. Therefore, the final stage of formation of the present-day biocoenoses began 2,500-3,000 years ago; thereby, the semidesert landscapes of the Ukraine, the north Caucasus, and the north Caspian began to change in the direction of a gradual conversion into steppes. With the humidification of the climate and the conversion of the landscape into steppes there was also a process of gradual change of the fauna under the influence of climatic factors and progressively increasing human activity.

It should be said that the idea of the existence of a xerothermic period as a universal phenomenon in the history of the earth is not generally accepted. I. G. Pidoplichko (1954) assumes that a certain "drying" of the climate could have occurred, but this "drying" was a regional phenomenon rather than a universal one. I. M. Gromov (1956a) believes that the regression of the Khavlynsk Sea signified the beginning of a change in the climate in the direction of a drying of it and a conversion of the landscapes into deserts. In his opinion, since the post-Khavlynsk era semideserts have

become the main landscape in the north Caspian.

With humidification of the climate the degree of development of agriculture increased notably, particularly in the vicinity of the seas, lakes and rivers. At the beginning of the present era in many regions of the south of the European portion of the USSR agriculture was a very well-developed branch of human activity, which is evidenced by the lively mercantile relations of the Black Sea area with the countries of western Europe, chiefly with Greece.

As is pointed out by M. I. Artamonov (1947) a tremendously important revolution occurred in the economy of the population of the southern half of eastern Europe. "At this time, on the basis of a generally uniform settled cattle-breeding-agricultural economy in accordance with different geographic conditions of the steppe and forest steppe strips of land two profoundly different types of economies were formed: cattle-breeding, migratory, in the steppes and settled agricultural economies with the use of the tractile power of cattle for cultivation of the land in the forest steppe strip" (page 70). By this time, apparently, a definitive differentiation had occurred in the zonality of the landscapes, which afterwards and continuing to the present day underwent changes chiefly under the influence of human activity. With the change in the climate and the formation of high-grass steppes, with the "thrust" of the forest toward the steppe (Tanfil'yov, 1894, 1928) and the intensification of human agricultural activity, the area of distribution of sousliks was reduced, whereby at the beginning of the present era it was, perhaps, considerably narrower than it is at the present time.

All this led to the formation of a souslik focus of plague within very narrow limits: the western border of it was probably Yergeni; the main source of plague infection in the Ukraine and in adjacent areas was the steppe marmot, which was better adapted to living in the tall grass steppes than the sousliks.

While in the Holocene, particularly in the xerothermic period, the tremendous natural European focus of plague probably had definite features of a multiplicity of hosts, now a considerable part of it has gradually been converted into a single-host type with the main source of the infection being the steppe marmot. Sousliks could no longer play a decisive part here in the establishment of plague not only because of the constriction of their area of distribution but also because souslik fleas were under very unfavorable ecological conditions (high degree of soil moisture) in connection with the formation of productive steppes, as is correctly pointed out by P. I. Shiranovich. In connection

with this, we cannot adopt the viewpoint of Yu. M. Rall' (1956) who, for some reason believes that sousliks displaced the marmots in the South of Europe and only the "final blow" was given to them by man.

Data in the literature attest to the fact that marmots in the southern steppes of Europe were present in abundance for a long time. As was noted by many investigators they were gradually exterminated by man or displaced by him during the course of his agricultural activity, and at the present time only separate colonies of these animals have remained in the region of the Don, in Kazakhstan and some other places.

I. G. Pidoplichko (1951) points out that even in the 19th century the marmots lived in the Zaporozhskaya, Stalinskaya and Poltavskaya Oblasts of the Ukraine, on the right bank of the Dniepr, and in other places. Before 1917 they lived near the village of Plissk in Chernigovskaya Oblast. In his time, N. A. Severtsov (1855) encountered steppe marmots in the eastern part of what was formerly Voronezhskaya Guberniya. As written by S. I. Ognev (1947) and A. P. Korneyev (1953), the French engineer Gisle de Wasser de Beauplan reported that in the middle of the 17th century he observed a tremendous number of horses and other animals as well as babocs [Marmota babak Müll.] on the left bank of the Dniepr, to the East of Cherkassy. At the end of the 18th century G. Gmelin encountered steppe marmots in large numbers on the Don. A. F. Flerov and V. N. Balandin (1931) point out that "50 years ago" in some regions of Severo-Kavkazskiy Kray hunting babocs was of the nature of a business. According to the report of P. Pallas (1809), he encountered a tremendous number of marmots between the Volga and the Dniepr.

The idea that marmots could be the main sources of plague infection in Europe for a long time has been expressed by V. N. Fedorov (1950), L. V. Gromashevskiy and G. M. Vayndrakh (1947), I. G. Pidoplichko (1951) and others. Pidoplichko reports that, judging by the data of archives (A. Kostyuchenko), the last marmot invasion of the Ukraine (in the region of Berdyansk) with a subsequent plague epidemic was observed in 1854-1855.

The process of complete disappearance of certain wild animals (particularly rodents, and reduction in the area of their distribution, as was indicated above, was connected not only with human activity but also with the change in the climate. As a matter of fact, it is difficult to conceive of the extinction, for example, of the yellow lemming or the steppe lemming over the broad spaces of the South Russian steppes as the result of their extermination by man.

A. N. Formozov (1938) believes that the extinction of

the yellow lemming occurred in less than a half century. The steppe cony lived in the Ukraine until 500 years ago. The great sand rat has been retreating to the East for 70-80 years, by approximately 200 kilometers. I. G. Pidoplichko (1930) believes that the steppe cony lived in certain areas of the UkrSSR a total of 150 years ago. We have already pointed out that S. I. Obolonskiy (1927) made an interesting finding of osteological remnants of the great sand rat on the right bank of the Volga, in the vicinity of North Zam'yana. It is difficult to judge whether these were remnants of an excavated form which died on the spot or whether the bones were brought there from the right bank of the Volga by chance, for example, by predatory birds; however, it is entirely probable that previously the great sand rat did live in certain places along the Volga (according to the verbal report of V. P. Babenyshev, O. N. Bocharnikov and V. M. Gusev, remnants of the great sand rat were also found in the Chernyye Zemli [Black Lands -- Caspian semidesert between Yergeni, the mouth of the Volga and the Caspian Sea]).

How can we explain the fact that despite the existence of an extensive natural focus of plague in southern Europe, reliable information about cases of plague among people here refer to a very late period, essentially to the sixth century A.D.?

First of all, it should be taken into consideration that medicine was so poor even in the middle ages, and the influence of religion and of the church was so great that the epidemic diseases including plague were described by the name of "pestilence" and were regarded by the population as an inevitable phenomenon, as "God's punishment" for the sins of people. However, there is no doubt of the fact that man was affected by plague very long ago, and epidemics of this disease were certainly widespread long before the "Justinian plague".

H. Stiker (1908) points out the existence of bubonic plague in 1060 B.C. on the shore of the Mediterranean Sea and in the Philistine cities of Gab, Echron, and Asdach, whereby the epidemic was associated with an "invasion" of mice. A number of other similar epidemics have been known in the various countries long before the sixth century A.D. Further, it should be taken into consideration that the territories included within the limits of the natural foci of plague were for a long time poorly inhabited by man, and the origin of cities was associated with the development of trade, that is, with the comparatively recent era in the history of development of human society (Rybakov, 1948 and others). Aeschylus (ancient Greek tragedian who lived from 526 to 456 B.C.) wrote the following about the south Russian steppes: "We

have arrived in a remote corner of the earth, in a Scythian land, in an uninhabited desert..." (from Latyshov, 1947, page 302). Nevertheless, the Scythian stage was characterized by the establishment of the present-day climate (by the advance of the forest into the steppe and conversion of part of the steppe into a forest steppe) and a mass conversion to the use of iron.

It must be supposed that in spite of the sparse, chiefly migratory population of the south Russian steppes before the period of their colonization, cases of plague among people as the result of contact with rodents did occur; however, active epidemics could not have developed because of the sparsity of the population. The localization of cases of the disease could occur for another reason. For example, there is information (Florov and Balandin, 1931) that the Polovites who lived for a long time in the south Russian steppes used sousliks as food and probably were not infrequently infected with plague from them. However, there is no information about epidemics among the Polovites, who frequently carried on military campaigns with large detachments.

It seems strange that epidemics did not develop amongthe Polovites in the presence of such intimate contact between them and sousliks. The probable explanation of this fact can be found in the following report by V. Rubruk (1911): "When someone (of the Polovites, N. M.) becomes sick, he is put into bed, and a sign is placed over his house that there is someone sick here and that no one should go in. Hence, no one visits the sick person, aside from those attending him. When a member of the great palaces becomes sick, for a great distance around the palace guards are placed who do not permit anyone to go beyond those limits. They are concerned specifically with whether those entering are not evil spirits or winds" (page 24).

Only with the growth of cities and the increase of the population in them could epidemics of large size develop, which could not be overlooked by either chroniclers or historians.

A characteristic description of a city in Russia in the feudal and early capitalistic periods is given by N. Kostomarov (1924). As a rule, the city was surrounded by wooden walls, in two, three or four layers, with spaces filled in with earth, which created favorable conditions for rat dwellings. Outside the walls close together and crowded into wooden houses with yards and gardens lived the lower middle class citizens, merchants, and the rest of the population. The common people lived in chimneyless huts, in an intolerable stench, with chickens, geese, pigs and calves. It becomes perfectly obvious why in the 14th century and for a

long time after it, until gradually expedient measures began to be used for controlling epidemics, plague so frequently ravaged the cities of Europe. About this subject A. Dieudonné and R. Otto (1928) correctly wrote: "In Europe, which during the centuries which followed (after the sixth century, N. M.) was visited again and again by epidemics, cases of plague in the middle ages became more extensive and more dangerous the greater the size of the population crowded in cities squeezed in by trenches and walls with narrow and dirty streets, in dark and stuffy houses" (page 2).

Note should be made of a single characteristic feature of historic references to plague epidemics in Russia. As a rule, they tell about the events in the largest cities. Most often, epidemics were described in Pskov, Novgorod, Moscow and Kiev. This is explained by the fact that epidemics in the large cities were a severe scourge to the entire government as a whole and were very important events in the life of the country. Outbreaks of plague in the small cities and other inhabited places occurred frequently unnoticed by history, although we cannot doubt the fact that these outbreaks, perhaps of local origin in the majority of cases particularly in semidesert and desert regions, were not an infrequent phenomenon.

While in the cities of north and middle Russia plague probably was of an imported nature, in the South, where natural foci of plague existed, many of the epidemics could have been of local origin. Specifically, within the limits of the present boundaries of Astrakhanskaya, Stalingradskaya, Rostovskaya oblasts and Stavropol'skiy Kray it is very probable that the following epidemics associated with the presence of a plague enzootic in sousliks and jirds, were of local origin (information about epidemics is given by F. Derbek (1905)): in the lowlands of the Volga region (particularly in Astrakhan') in 1656; in Astrakhan', in 1657, 1692, 1727-1730; on the Don (Azov) in 1739; in Taganrog and on the Don in 1771; in Taganrog, Kizlyar, Mozdok in 1773, etc.

It is characteristic that in the 19th century, when government and public measures for the control of plague had been given a definite impetus, the epidemics were limited and localized in the southern and southeastern portions of Russia, that is, in the immediate vicinity of the natural foci of plague infection. The plague epidemic which began at the end of the 18th century lasted, with brief interruptions, until 1819 in the Caucasus (Tiflis, Imeretiya, Gori, Kabarda, Georgiyevsk). In 1805, plague appeared in the North Caucasus, and then in Astrakhanskaya Guberniya among the Tatars who lived near the port and in the village of Tsarevskiy near Astrakhan'.

In 1807-1812 plague was recorded in Mozdok, Kizlyar, and in Stavropol'skiy district. In 1807-1808 the plague epidemic occurred in Saratovskaya Guberniya, and in 1816, in Stavropol', and then in Mozdok, Astrakhan' and Krasnyy Yar. In 1824 plague appeared in the Caucasus in the vicinity of Erzorum, and in 1825 it appeared in Yerevan. After a short interval plague epidemics were again noted in the Caucasus during the period between 1838 and 1843.

After 1877-1879, when the epidemics were recorded in Vetlyanka, Prishib, Yenotayevsk, Nikol'sk and other inhabited places, plague did not once occur in Astrakhanskaya Guberniya. A number of plague outbreaks in the 19th century were also noted in the Ukraine, in the Crimea, and in Moldavia.

Attention should be directed to the fact that the plague epidemics in the area of the steppes, particularly in the Ukraine, stopped considerably earlier than they did in the semidesert zone (that is, in Astrakhanskaya and Stalingradskaya oblasts and Stavropol'skiy Kray), unless we take into consideration cases of imported plague, for example, in Odessa. This can be explained only by the fact that the basic factors in the natural focalization of plague in the steppe zone in the middle of the 19th century were already essentially completely eliminated as the result of human agricultural activity.

The process of reclaiming the steppes by man in its general outline can be followed on the basis of data concerning the growth of the agricultural population in the steppes of South Russia.

Almost until the 17th century the steppe region of Russia was poorly inhabited by man; therefore, his influence on vegetation and various types of wild animals, which were distinguished by a relatively high census (for example, rodents) was extremely slight. It must be supposed that at that time the open spaces of the greater part of the Ukraine, Rostovskaya Oblast, Stavropol'skiy Kray and other such areas constituted limitless virgin territories covered by lush steppe vegetation.

A. F. Florov and V. N. Balandin (1931) point out that five or six hundred years ago the steppes of the Severo-Kavkazskiy Kray were covered by a vast sea of grass. These were strips of territory which had a very sparse settled population scattered throughout the small cities, villages and farmsteads. Our forebears called these steppes "fields", "wild fields". V. V. Dokuchayev (1953), studying the degree of influence of human agricultural activity on the virgin nature of the steppes, wrote the following: "...unfortunately, now only pitiful shreds had remained of the typical steppe flora which once solidly covered the chernozem steppes".

According to the evidence of historians (see, for example, M N. Tikhomirov and S. S. Dmitriyev, 1948), at the end of the 16th century a considerable increase of the population was observed in the middle Volga area, on the Don, in the Ukraine, which is explained by the flight of peasants and partly of tradespeople from their old places to the periphery in search of freedom from feudal exploitation. In the middle of the 17th century the Don Cossacks inhabited the basins of the lower course of the Don. Here and to the lower Volga region a tremendous number of refugee peasants came. In connection with the need for bread there was a marked increase in the plowing of virgin territory. In the first half of the 18th century in the Ukraine large estates of Russian landowners began to be created, and in the beginning of the 19th century agricultural specialization of various regions of the country came out distinctly. In the southern and western regions chiefly agriculture and cattle breeding developed. The expansion of internal and foreign markets required an increase in goods production, in connection with which there was a marked increase in work done by serfs for their lords and there was a rapid growth of the area of seignorial land for plowing.

In the first half of the past century a particularly vigorous process of colonization of the southern steppes of European Russia began. The landowners resettled the peasants on territory bestowed upon them in whole villages. By 1819 the population of the steppe Ukraine already amounted to about 3,000,000 persons (History of the USSR, Vol II, 1949). The rates of development of capitalism in the Ukraine and North Caucasus were particularly rapid. This is explained by the fact that these regions were located close to seaports and markets and that there were far fewer remnants of feudalism here than in Central Russia.

In the second half of the 19th century the Ukraine had become one of the leading places with regard to the production of commodity grain. During this period tremendous masses of peasants resettled in the Ukraine. In the book, "Development of Capitalism in Russia", V. I. Lenin points out that by 1890 the main production center for grain had been shifted from the central chernozem guberniyas to the steppe and lower Volga guberniyas. "The abundance of free land," wrote V. I. Lenin, "attracted a tremendous inflow of colonists here, who rapidly expanded the plantings" (page 218). Between 1885 and 1897 hundreds of thousands of peasants resettled here.

A graphic example of the intensity of colonization of the southern steppes of Russia in the second half of the 19th century is constituted by data concerning the growth of Stavropol'skiy Guberniya from settlers coming from Central Russia.

According to the data of K. Slavskiy (1914), the dynamics of increase of the population in Stavropol'skiy Guberniya from 1873 through 1909 are expressed by the following figures:

In 1873 there were 475,051 persons

In 1881 there were 589,951 persons, an increase of 114,900 persons,

In 1889 there were 626,014 persons, an increase of 36,063 persons,

In 1897 there were 873,301 persons, an increase of 247,287 persons,

In 1909 there were 1,170,339 persons, an increase of 244,038 persons.

In 36 years the population of Stavropol'skiy Guberniya had increased by two and one-half times.

As the result of an active process of colonization of the periphery of Russia during the century or two which passed there was a radical change in the landscape of the steppes. Because of extensive fields of grain the virgin territory was converted into small sections adjacent to inhabited places, roads, gullies, etc., while the marmots, as the most probable sources of plague, were crowded out and exterminated here by man permanently. In these regions where the sources of plague infection might have been the sousliks (Crimea, North Azov area, the relatively low-grass sections in the steppe zone), the latter were also graduall crowded out into limited areas of virgin territory in the form of pasture land, shoulders of roads, etc., as the result of which prolonged maintenance of the plague pathogen proved to be impossible among their population.

Therefore, it becomes obvious that the main cause of quiescence of the natural plague focus in the extensive territories of the tall-grass steppes in the south of Russia was human agricultural activity.

For the purpose of understanding the further history o establishment of the plague focus in northwest Caspian area it is essential to take into consideration two very important and, to a certain degree, opposite processes. In the steppe regions of the country, where the main trend of huma activity was the growing of grain (the Ukraine, the right-bank and partly the left-bank areas of the lower Don, and the northern part of the lower Volga) the process of expanding the "cultivated" landscapes proceeded, which led to a reduction in the areas of distribution of rodents--the sources of plague infection (sousliks)--or almost complete disappearance of them (marmots).

In the semidesert regions and in regions which had transitional features between semideserts and steppes, wher

the main trend of the economy was a migratory and a driving type of cattle breeding or agriculture and cattle breeding with primacy of the latter (Astrakhanskaya Oblast, southern rayons of Stalingradskaya Oblast, the northern rayons of Stavropol'skiy Kray), conversely, the process of xerophytization of the steppes proceeded quite rapidly, leading to an increase in the census and expansion of the areas of distribution of such species of rodents as the dwarf souslik, meridional and crested jirds, and others. Excessive grazing of cattle on sandy soils, in addition, led to exposure of the sand and, therefore, to an increase in the census of sand-dwelling rodents.

Judging by the investigations of K. Ya. Pirkovskiy (1914), before the beginning of the present century almost all of the rayons of Rostovskaya Oblast and Stavropol'skiy Kray on the right bank of the Volga were free of sousliks. In the northwest Caspian region their southwest boundary was essentially Yergeni, where the colonies of those animals, considering the sizes of their hills, are very ancient. Active development of cattle breeding and unplanned excessive grazing of the cattle led to denuding many steppe regions of Rostovskaya Oblast and Stavropol'skiy Kray, as the result of which beginning with the end of the 19th and the beginning of the 20th century a marked expansion of the boundary of the area of distribution of sousliks was observed in the southern and southwestern directions.

S. M. Nikanorov (1923) points out that in the vicinity of the villages of Zavetnyy, Fedosoyovka and Kichkin in Rostovskaya Oblast sousliks appeared at the end of the past century, whereby the expansion of the area of distribution of this rodent was connected by the author with the replacement of the lush vegetation of the Don steppes by sparse and motley grass vegetation. According to the data of K. Z. Zavarzina and V. I. Kuzenkov (1929) as well as of O. N. Bocharnikov (1946), the appearance of sousliks in the eastern rayons of Rostovskaya Oblast refers to the beginning of the present century. In Remontnenskiy Rayon the first appearance of sousliks was noted in 1908-1909, and in the environs of Zimovnikov, only in 1919-1920. As is pointed out by V. N. Zryakovskiy (1926) and V. M. Belousov (1933), a particularly active advance of sousliks into the depth of cultivated areas was noted in the drought years of 1924 and 1925.

In the last 40-50 years the sousliks have advanced to the West and Southwest 300 kilometers, settling in an area of about 10,000,000 hectares (Sviridenko, 1927; Romanova, 1936; Babenyshev, Birulya and others, 1937; Mironov, Pavlov and others, 1952; Babenyshev, 1956).

N. Osorgin (1910), P. Yerofeyev (1926), I. G. Ioff

(1936) and others point to expansion of the boundaries of the area of distribution in the northern portion of it. The fact of expansion of the area of distribution of sousliks confirms our conclusion that after the xerothermic period for many hundreds of years the natural focus of plague in the northwest Caspian region has been in a very much reduced state. Until the end of the 19th century and beginning of the 20th century it was limited to the right-bank area of Rostovskaya Oblast, the southeastern rayons of Stalingradskaya Oblast, and certain rayons of Stavropol'skiy Kray located to the north of the Kuma River. Therefore, the part of the present-day focus which includes the eastern rayons of Rostovskaya Oblast and the northern regions of Stavropol'skay Kray and Groznenskaya Oblast (to the south of the Kuma River) were, essentially, "plague infested" secondarily after the xerothermic period in connection with the expansion of the area of distribution of sousliks.

Therefore, the ecological factors which have contributed to the occurrence of a plague enzootic in the present-day era and which involved afterwards very serious epidemic complications are the products of recent times. It should be noted that the eastern boundary of the focus in the northwest Caspian region, adjacent to the sea, is not a permanent one. Even in the modern era it not uncommonly has changed in connection with the variations in the Caspian basin, whereby these changes have always inevitably reflected on the census of the main species of rodents in the area near the sea, particularly on the census of jirds and great sand rats.

In the xerothermic era, as is pointed out by L. S. Berg (1943), the level of the Caspian Sea occupied a very low position, and from the geological viewpoint in the current era the Caspian has been in the stage of transgression, which is evidenced by Bera's mounds [sand dunes from six to 22 meters in height along the north shore of the Caspian Sea and near the Volga delta, extending in stretches from 200 to 400 meters; first described by Bera in 1856, there are seven different hypotheses of their origin] on the sea bottom before the Volga delta as well as ilmenium deposits.

According to the data of V. D. Zaykov (1946), beginning with 1830 a steady decrease in the level of the Caspian Sea has been occurring from year to year, unless we take into consideration the greatest elevations in 1932-1933 and 1942-1944. By 1946 the secular reserves of the sea had been reduced by 750 cubic kilometers; the shoreline on the north shore of the Caspian had receded in the direction of the sea by tens of kilometers, and the area of the sea had been reduced by approximately 28,000 square kilometers. A particularly rapid drop in the level of the Caspian Sea has been observed

from 1932 through 1941. As is indicated by B. A. Fodorovich (1950), during this period the sea level has dropped by almost two meters.

An oven lower position of the Caspian Sea during the period of history occurred probably at the beginning of the 13th century, which is evidenced by a fortress, built at about that time, in Babinskaya Bukhta [bay] not far from the shore. This structure has recently been found in the form of half-flooded ruins. The highest level of the Caspian Sea was observed in the 18th century and at the beginning of the 19th century; the lowest level after the 13th century (but considerably higher than the present-day level) was in the first half of the 16th century.

Therefore, recently we have been the witnesses of an expansion of the focus of the northwest Caspian in its eastern portion, particularly since in recent years an expansion of the areas of distribution of sousliks and great sand rats and jirds has been noted in the direction of the sea. However, in the past 20-25 years plague organizations of the northwest Caspian have done tremendous work on the control of the main source of the plague pathogen, the dwarf souslik. At the same time, another very important process has occurred, agricultural reclaiming of virgin steppes for arable land, gardens, forest belts, etc. As the result of this, a large part of the natural focus of plague in the northwest Caspian (with the exception of the Black Lands, the eastern rayons of Groznonskaya Oblast and the lowlands of Dagestan) at the present time may be considered practically free of the pathogenic agent of this infection.

This is a brief probable history of the occurrence and establishment of the focus in the northwest Caspian region, based on current concepts of the factors of the natural focalization of plague infection. This history is evidence to the effect that this focus is a remnant of what was once a tremendous focus of plague occupying all the southern steppes of Europe, and that we are living in a period of its final extinction. The acceleration of this process depends a great deal on us, the plague workers.

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969

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6964

pp 54-64

Rules and Regulations of a Plague Enzootic in a Focus in the Northwest Caspian Region

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In the report the results of many years of study of a natural plague focus in the Northwest Caspian Region, made by a large number of investigators, are being generalized on. Aside from the authors of the report, the rules and regulations of focalization and epizootology of plague in this territory have been studied by O. A. Aristarkhova, V. S. Grikurov, I. G. Ioff, N. I. Kalabukhov, V. I. Kuzenkov, S. M. Nikanorov, M. P. Pokrovskaya, V. V. Rayevskiy, P. N. Stupnitskiy, S. V. Suvorov, V. Ye. Tiflov, V. M. Tumanskiy, B. K. Fenyuk, A. A. Flegontova, A. A. Churilina and many others.

An essential influence on the formation of certain views about the focus in the Northwest Caspian Region has been exerted by the study of other natural plague foci in the USSR and foreign countries. This applies chiefly to the Volga-Ural natural focus of plague which is adjacent to the focus in the Northwest Caspian Region and is located in general in the same climatic zones; this was studied by a number of the persons mentioned above as well as by some authors of this report, and in addition by A. I. Bordnikov, N. A. Gayskiy, I. A. Dominskiy, N. N. Klodnitskiy, S. A. Kolpakova, G. I. Kol'tsov, I. M. Mamontov, Yu. M. Rall', M. M. Tikhomirova, I. I. Tikhomirov, V. N. Fedorov and others.

In making out this report each author formulated chiefly those sections dealt with by the materials of his own research. At the same time, on the main problems there was coordination between all the authors. The last names of the authors of the report are given in alphabetical order.

The beginning of the study of the rules and regulations of the plague enzootic in the Northwest Caspian Region was in 1913, at a time when investigators in plague institutions, working according to plan and under the direction of Academician D. K. Zabolotniy, isolated cultures of the plague microbe from wild rodents for the first time in this focus. Subsequently, since the focus continued to be active, and before work done on the elimination of it, that is, prior to 1933-1934, it was very active, the isolation of plague cultures from rodents and their ectoparasites was repeated regularly from year to year. In all, in the period from 1913 through

1936 epizootics among rodents were found in the focus more than 700 times. In many places they were demonstrated repeatedly, sometimes for several years straight or with some interruptions; in others, they were recorded as a one-time phenomenon.

The great majority of the plague microbe cultures was obtained from dwarf sousliks and their fleas. These cultures could be isolated regularly during the spring-summer period. At the same time, cultures of the plague microbe from souslik fleas were obtained in the autumn and winter, although in isolated cases.

Much less often, cultures of the plague microbe were isolated from crested and meridional jirds [Meriones tamariscinus and Meriones meridianus] and from their fleas, whereby those facts were recorded in far from all places and usually with great intervals of time between individual epizootics in populations of these species of rodents. Within the limits of the greater part of the area of distribution of jirds in the Northwest Caspian Region plague cultures from those animals and their fleas were not isolated at all. In the eastern part of the Black Land Region they were isolated only in the spring-summer season and only in the il'men-delta subzone were the infected jirds and their fleas found in the autumn-winter period also.

From house mice in large numbers plague microbe cultures could be obtained only in the autumn-winter of 1932/33 and 1933/34 during a period of mass multiplication of mouse-like rodents. In other years cases of isolation of cultures from mice were scattered.

Cultures of the plague microbe in this focus were also isolated from jerboas, Siberian polecats and camels.

Many years of observations of the focus demonstrated its natural boundaries, which from 1913 through 1956 have changed several times. From a historical aspect, in summing up all the areas on which the plague enzootic has been demonstrated during this time in the form of epizootics among rodents, the focus has included the following territories of the Northwest Caspian Region.

The northern boundary of the focus in 1913 passed only 12 kilometers to the south of the city of Tsaritsyn (now Stalingrad), but even in the 1920's to the beginning of the 1930's, apparently as the result of the expansion of plowing and the increase in the number of inhabited places near Stalingrad, the northern boundary of the focus dipped 40 kilometers to the south, becoming stabilized along the Mishkova River.

The eastern boundary of the focus during all the periods of its modern history was the Volga River and the northern

part of the western coast of the Caspian Sea. The southern boundary was constituted by the steppes of the Manych lowland, to the north of Manych and the Kuma River, which evidently was associated with the absence or small population of dwarf sousliks at the beginning of this century in the Pre-caucasian steppes, to the south of those water bodies. In precisely the same way the southwestern boundary of the focus coincided with an area of marked reduction in the souslik census in the Sal'skiy steppes to the south of the villages of Romontniy and Zavetnoye, although to the north it passed along the shore of the Don River.

At the beginning of the 20th century a successive expansion of the boundaries of the focus in the Northwest Caspian Region was noted in the western and southern directions (Fig. 1) as the result of expansion of the area of distribution of the dwarf souslik. As the result of the latter, conditions were created by the 1930's for the circulation of the plague pathogen in the eastern rayons of Rostovskaya Oblast (Dubovskiy, Zimovnikovskiy, Martynovskiy, Krasnoyarskiy) and in the northern rayon of Stavropol'skiy Kray to the south of Manych. Even later, as early as the 1950's the focus was extended to the south of the Kuma River, into the depth of the steppes of Groznenskaya Oblast and into the pla' of Dagestan. Such an extension of the focus was observed somewhat earlier to the East, on the territory from which water had been cleared as the result of the sharp drop in the level of the Caspian Sea in the past 50 years. Therefore, during the period of the most recent history of the focus in the Northwest Caspian Region the oldest parts of it were Yergeni and the Priyergeninskaya Ravnina [plain], and the youngest areas, formed even within the present century--the eastern rayons of Rostovskaya Oblast, the northern rayons of Stavropol'skiy Kray (to the south of Manych) and Groznenskaya Oblast as well as the entire northwestern strip of Primor'ye (Caspian), including the plain area of Dagestan.

Retrospective analysis of an abundance of indirect data permits us to believe that the plague focus in the Northwest Caspian Region is a relict of a tremendous natural focus, in its current boundaries, which at one time occupied the steppes of Southern Europe. The formation of the latter can be referred to the middle Pleistocene, that is, to the time about 80,000-100,000 years ago. Since that time, undoubtedly, repeated changes in the size of this focus have occurred associated with climatic changes and variations in the levels of the Caspian and Black Sea basins. About 3,000 years ago, after the xerothermic period a process of formation of tall-grass steppes occurred over the greater part of Southern Europe, as the result of which a differentiation occurred of

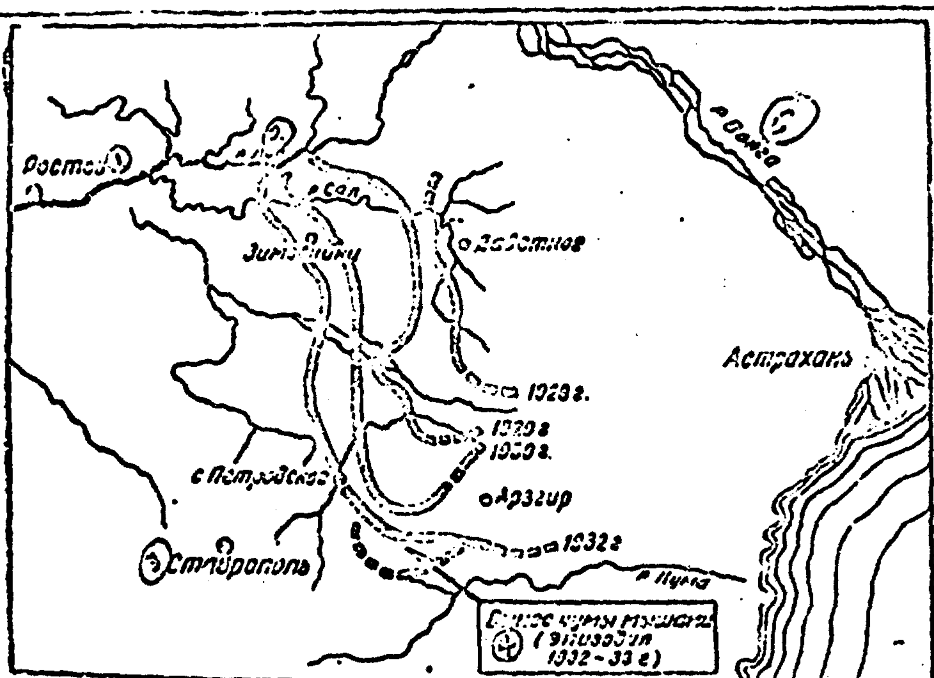

Fig. 1. Change in the Southern and Western Boundaries of the Enzootic Territory of the Focus in the Northwest Caspian Region from 1928 through 1932 (according to B. K. Fonyuk, 1947, Manuscript). 1. Rostov; 2. Don River; 3. Stavropol'; 4. Carriage of Plague by Mice (Episode of 1932-33); 5. Volga River.

what apparently previously was a multiple-host focus of plague in Europe; in the western part of it marmots now became the main sources of the pathogen of the infectious disease; in the eastern part (Yergeni and the Priyergeninskaya Ravnina [plain]), sousliks became the main reservoirs.

During the course of active colonization of the southern rayons of Russia in the 18th-19th centuries the landscape of the steppes was fundamentally changed. As the result of human agricultural activity the steppe marmots were directly or indirectly almost completely exterminated, while the European natural focus of plague was reduced to very small dimensions: its western boundary was now Yergeni; southern boundary, Kumo-Manych Valley; and northern boundary, the latitude of the southern suburbs of what is now Stalingrad.

At the present time, the rodent fauna of the Northwest Caspian Region is represented by the following basic 22 species of rodents (Table 1).

Table 1.

№	Вид грызуна	Встречаемость в различных подзонах							
		Ергени	лощина Дабан	побережье Волги	Приволжские пески	Ильменя-дельтовая подзона	Приморье	Кумо-Манычская подзона	Черные земли
1	Суслик малый	0	++	++	+	+	++	++	0
2	Песчанка гребенщиковая	—	—	+	++	0	++	0	++
3	Песчанка полуденная	+	+	+	0	+	++	++	++
4	Мышь домовая	++	+	++	++	++	+	+	+
5	Крыса серая	—	—	+	+	++	—	—	—
6	Мышь полевая	+	—	+	+	+	—	—	—
7	Мышь лесная	+	—	+	—	+	—	—	—
8	Полевка обыкновенная	+	—	+	+	++	+	+	—
9	Полевка общественная	+	+	+	+	+	++	++	++
10	Слепушонка обыкновенная	+	+	+	+	+	+	+	+
11	Пеструшка степная	+	+	+	—	—	—	+	+
12	Полевка водяная	+	—	+	—	++	—	—	—
13	Хомячок серый	+	+	+	+	+	+	+	+
14	Хомяк обыкновенный	+	—	+	—	—	—	+	—
15	Слепыш обыкновенный	+	—	—	—	—	—	+	—
16	Мышовка южная	+	+	+	+	+	+	+	+
17	Тушканчик большой	+	+	+	+	+	+	+	+
18	Тушканчик малый	+	—	+	+	+	+	+	+
19	Тарбаганчик	+	+	+	+	+	+	+	+
20	Емуранчик	+	+	+	+	++	++	+	+
21	Тушканчик мохноногий	—	—	—	+	+	+	+	+
22	Заяц-русак	+	+	+	+	+	+	+	+

[Along the Horizontal]. 1. Species of Rodents; 2. Incidence with which it is found in various subzones; 3. Yorgoni; 4. Daban ravine; 5. Banks of the Volga; 6. Volga sands; 7. Il'men-delta subzone; 8. Primor'ye; 9. Kumo-Manych subzone; 10. Black Lands. [Along the Vertical]: 1. Dwarf Souslik [Citellus pygmaeus]; 2. Crested jird [Meriones tamariscinus], 3. Meridional jird [Meriones meridianus]; 4. House mouse; 5. Brown rat [Rattus norvegicus]; 6. Field mouse; 7. Wood mouse [Mus sylvaticus]; 8. Common vole [Microtus arvalis]; 9. Social vole [Microtus socialis]; 10. Mole vole [Ellobius talpinus]; 11. Steppe lemming [Lagurus lagurus]; 12. Water vole [Arvicola terrestris]; 13. Gray hamster [Cricetulus migratorius]; 14. Common hamster [Cricetus cricetus]; 15. Mole rat [Spalax microphthalmus]; 16. Birch mouse [Sicista]; 17. Allactaga [Allactaga jaculus]; 18. Dwarf jerboa [Allactaga elater]; 19. Tarbagan [Marmota sibirica]; 20. Jerboa [Scirtopoda telum]; 21. Hairy-footed jerboa [Dipus sagitta]; 22. Common hare [Lepus europaeus].

Key: (-), species absent; (++), common; (+), present in small numbers; (0), abundant.

As is seen from the general data presented in Table 1, the most abundant species of the rodents in the majority of rayons of the Northwest Caspian Region is the dwarf souslik. In some eastern rayons of the focus the jirds are present in relatively large numbers. There is an increased census of mouse-like rodents, particularly the house mouse, recorded most often in various years in Yergeni and to the west of it, along the banks of the Volga and in the il'men-delta subzone. [A geographic subzone is part of a geographic zone which has definite zonal landscape characteristics; an il'men is a shallow water lake without sharply defined banks, densely overgrown with reeds.] Local conglomerate foci are formed also by the jerboas (il'men-delta subzone) and the social vole (Microtus socialis) (Black Lands, Kumo-Manych subzone, Primor'ye). The other species are relatively few and are not of essential epizootological significance.

Within the limits of the Northwest Caspian Region there are more than 50 species of fleas, of which about 40 species are parasitic on rodents. The most common species are the following: a) souslik parasites--Neopsylla setosa, Ceratophyllus tesquorum, Frontopsylla semura, Ctenophthalmus pollex, Oropsylla ilovaiskii and some others, and b) mouse and vole fleas--Ceratophyllus mokrzeckyi, C. consimilis, Leptopsylla segnis, Ctenophthalmus secundus and some others.

Of the jird fleas the most abundant are: Ceratophyllus laeviceps and Rhadinopsylla cedestis; less often encountered is Rhadinopsylla bivirgis; very rarely, Xenopsylla conformis as well as Stenoponia vlasova Coptopsylla bairamaliensis; and, finally, in isolated specimens Ctenophthalmus dolichus and Coptopsylla lamellifer are found.

Jerboa fleas are quite common: Mesopsylla hebes, Mesopsylla eucta tuschkan and Ophthalmopsylla volgensis. In the Sal'skiy steppes and further to the West Ctenophthalmus orientalis is common, which is parasitic on sousliks, voles and other rodents which inhabit the steppe areas. In the river basis of the Volga, Don and other meadow areas Ctenophthalmus wagneri and fleas of wood mice of the forest steppe zone and the foothills of the Caucasus, Leptopsylla taschenbergi, are found.

The synanthropic flea Pulex irritans, which at one time was very abundant in human dwellings and buildings, has been exterminated recently with the introduction of synthetic insecticides and is practically absent from the Northwest Caspian Region. Even in primitive human dwellings, of the mud-hut type, fleas are practically never encountered.

Part of the species listed is very common on the territory of the Northwest Caspian Region and is distinguished by a stable or permanent high seasonal census. Among them

are chiefly souslik fleas, N. setosa and C. tesquorum. Just as common are the fleas of mice and voles which are distributed very irregularly, and their census undergoes marked variations and in various years drops to an extremely low level.

Another group of species goes beyond the limits of the Northwest Caspian Region only in a part of its area of distribution (for example, fleas of jirds, wood mice) or is encountered sporadically in isolated cases, or else is scattered over the entire territory in small numbers.

In a zoogeographic sense the fleas of the Northwest Caspian Region are of a mixed character and are different in their origin. Along with well-represented autochthonous (for example, the majority of species of souslik fleas), cosmopolite and palearctic types, here representatives of the Central Asiatic deserts, Central Russian and South Russian plains, and foothills of the Caucasus are represented. A considerable part of the flea species of the Northwest Caspian Region must be considered as belonging to the Aral-Caspian fauna.

Many years of observations made in this focus have shown that active epizootic plague processes among souslik populations occurs only during the periods of their activity. Thereby, after the sousliks come out of their hibernation and until the period of the beginning of dispersal and settlement of the young sousliks in their separate nests, as a rule, only sporadic cases of plague are encountered among them.

In the nature of the Northwest Caspian Region an active epizootic process comes about in the spring-summer period and lasts a total of only 30-45 days. The beginning of the active course of the epizootic among sousliks coincides with the beginning of dispersal and settlement of the young individuals from their maternal nests to individual holes. During the period of the active course of the epizootic among sousliks the highest percentage of plague-infected individuals is encountered, and at that time mass deaths of them occur from plague.

The calendar periods of occurrence of the active epizootic process, just like the times of all periodic phenomena of souslik activity, depend chiefly on the time and duration of the period of awakening of the animals from their hibernation (Fig. 2).

This fact is of more than a little importance for making an appropriate epizootological prognosis, which under conditions of an active focus can be quite accurate if careful observations are made of the course of awakening of sousliks from their hibernation.

The dying down of an active epizootic usually coincides

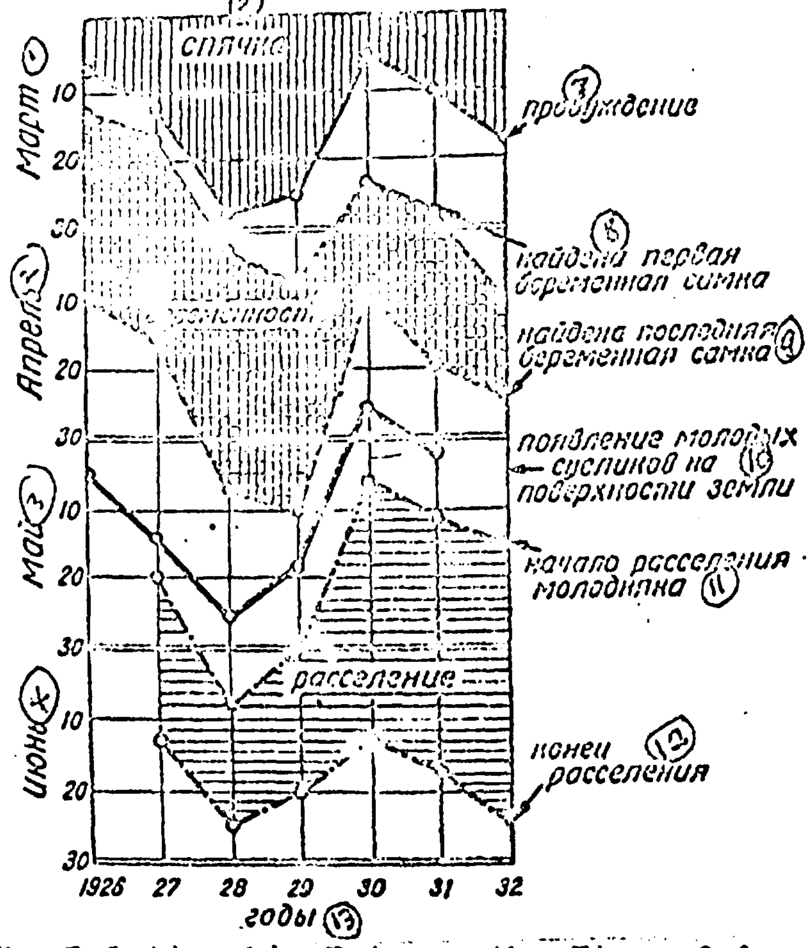

Fig. 2. The Relationship Between the Time of Occurrence of Various Biological Phenomena in Dwarf Sousliks and the Time of Their Awakening from Hibernation (According to N. I. Kalabukhov, 1956). 1. March; 2. April; 3. May; 4. June; 5. Hibernation; 6. Gravidity; 7. Awakening; 8. First Gravid Female Found; 9. Last Gravid Female Found; 10. Appearance of Young Sousliks on the Surface of the Earth; 11. Beginning of Dispersal and Settlement of the Young; 12. End of Dispersal and Settlement; 13. Years.

with the period when the young sousliks born in the current year dispersed completely and settled in their respective holes, when the old males began their hibernation, and the old females had become fat and also lay down to hibernate (Fig. 3).

The considerable factual material obtained from the investigation of rodents caught under natural conditions of the focus is evidence of the fact that the portals of in-

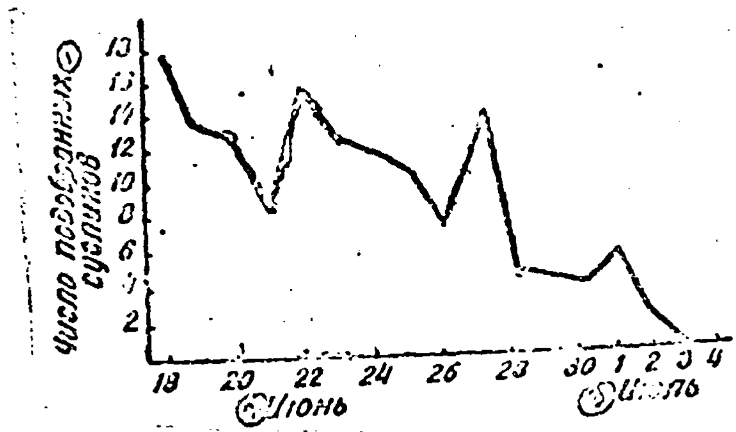

Fig. 3. The Course of a Plague Epizootic in a Dwarf Souslik Population, as Determined by Means of Collecting Sousliks Which Died of the Plague (after I. S. Tinker, 1940). 1. No of Sousliks Collected; 2. June; 3. July.

fection in sousliks are most often or almost exclusively the skin. This becomes clear from the predominance of bubonic and septic forms of the plague, in which transmission of the pathogen is accomplished through living vectors.

Actually, in the area in which active epizootics of plague occur in sousliks it was very easy to find plague-infected fleas in the nests, holes and on the animals themselves, which insects were found to be infected in 50 percent of the cases or even more.

As time passed after the end of the active course of the epizootic the number of fleas infected with the plague pathogen, considered with respect to their total numbers, decreased. However, scattered specimens of fleas were recorded in na[illegible] two, four and even eight months after the active epizootic had died off in the gastrointestinal tracts of which the plague microbe was found.

It should be emphasized that not all the species of fleas listed above can be considered active plague vectors.

On the basis of observations in nature, experimental study of the role of fleas as vectors of the plague microbe and consideration of ecological characteristics of various species of fleas, only the following fleas may be considered a belonging to the group which is most important in an epidemiological respect: N. setosa, C. tesquorum, C. mokrzeckyi, C. consimilis and C. laeviceps. Souslik fleas--N. setosa and C. tesquorum-- which have a high potential in transmitting the plague microbe and are capable of preserving

it for a long time in their bodies are common over the entire territory of the focus and are characterized by a high census, although it changes according to seasons. In the autumn, winter and early spring there is a predominance of the moisture-loving nest flea N. setosa, but towards summer its census falls off markedly. By this time a mass production of fleas occurs from the fur of the host--C. tesquorum--and at the time of dispersal and settlement of the young sousliks this species becomes prevalent.

In the plague focus of the Northwest Caspian Region it has been determined that souslik fleas of the species N. setosa survived throughout the entire interepizootic period. They are responsible for the carriage of the plague pathogen from one epizootic season to the next.

Among jird fleas under conditions of the Northwest Caspian Region only one species, I darosay, can be of some epidemiological significance--C. laeviceps--the census of which on the right bank of the Volga River is generally much less than on the left bank, although in various years the indices for this species in the spring and autumn can reach considerable figures, particularly on the crested jirds.

An active plague vector--X. conformis--as has been mentioned above, is encountered extremely rarely on the right bank of the Volga, and in various years is practically absent on jirds which live in small areas of the sands and particularly at the fringe of them or in the steppes. Souslik fleas are numerous, and in some biotopes the fleas of jerboas, mice and voles are also abundant.

Of the fleas of the small mouse-like rodents C. mokrzecki--the house mouse flea--and C. consimilis--the vole flea--may be of some significance, chiefly in the steppe area. During the years of mouse invasions the census of these species increases considerably, and then they can penetrate into inhabited places and settle in human buildings.

The natural characteristics of the plague focus in the Northwest Caspian Region are very dissimilar in their various parts, which to a considerable degree is responsible for the nature of the course of the epizootics and serves as a definite indication of the degree of strength of the plague enzootic factors. On the basis of these features, with consideration of the species composition and the rodent census and the census of their ectoparasites we may distinguish the following most important natural-historic regions (subzones) of the focus (Fig. 4).

A mosaic landscape is characteristic of Yergeni and the Western Yergeni steppes--the alternation of semidesert elements with steppe and "cultivated" elements in the form of the bottoms of valleys, cultivated lands, plantations, melon

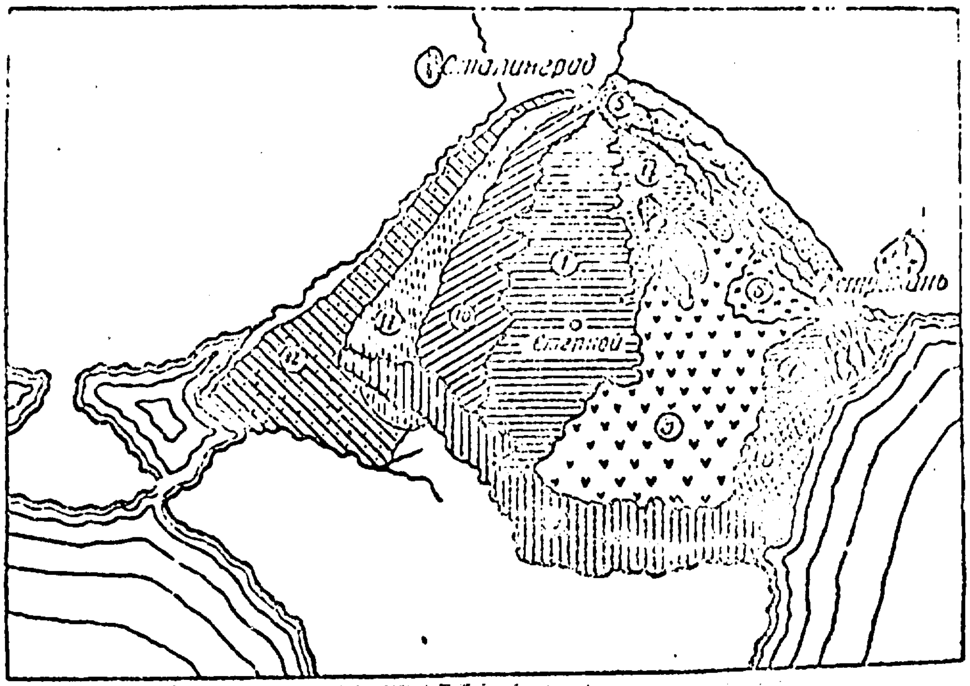

Fig. 4. Diagram of Landscape-Ecological Zoning of the Northwest Caspian Region within the Limits of the Volga-Don Watershed and the Area Between the Volga and Kuma Rivers. A. Semidesort Zone. 1. Yergeni; 2. Dabanskaya Loshchina [ravine]; 3. Black Lands; 4. Northern Lowland Steppes; 5. Coastal Volga Steppes; 6. Volga Sands; 7. Il'men-Delta Region; 8. Primor'ye; 9. Kumo-Manych Region; B. Area of Dry Steppes (Western Yergeni Steppes); 10. Wormwood-Sheep's-Fescue Steppes; 11. Sheep's-Fescue-Feather Grass Steppes; 12. Chestnut-Chernozem Steppes; 13. Stalingrad; 14. Astrakhan'.

fields, etc. In connection with this, here active summer migrations of sousliks are noted which provide an exceptionally close intraspecies contact between the animals. The Black Lands, conversely, are distinguished by a relatively uniform landscape, which excludes such active migrations of sousliks as in the previous area. On the sandy and sandy loam soils of the Black Lands, in contrast to the majority of other regions, a seasonal duration of the souslik holes is noted, in which, as a rule, toward July, August capacious probes are formed in the earth. As the result of this, toward the end of the summer intraspecies contact between sousliks falls off sharply, and interspecies contact is practically inter-

rupted. This leads to a complete extinction of the epizootics, because of which searches for infected rodents and their ectoparasites in the Black Lands in the autumn-winter, as a rule, gave no results. In the il'mon-delta region, which is distinguished by an exceptionally variegated landscape, almost all species of rodents are very mobile and are constantly in close contact with one another. Characteristic of this region are also insular colonies of the meridional and crested jirds and a considerable variety of rodents and their ectoparasites. The other regions occupy a kind of intermediate position, in their natural characteristics, between the areas described, showing different degrees of similarity to the latter.

The rules and regulations of the epizootic process in different areas of the focus in the Northwest Caspian Region were different and varied in accordance with the natural features, the ecology of the hosts of the plague pathogen and its living vectors on each of the areas and in each season of the year. Here, two main forms of circulation of the plague microbe were noted.

The first form is responsible for an active epizootic. In it, an acute infectious process develops in the hosts of the pathogen quickly and terminates fatally with signs of agonal septicemia. This leads to a high degree of infection of the fleas, which are capable of transmitting the plague pathogen effectively. Such epizootics, as a rule, occurred in the spring-summer season among the sousliks in Yergeni and in the Western Yergeni steppes.

The high degree of motor activity of sousliks, frequent and distinct active and passive movements of the fleas assured an active intraspecies contact between the fleas of the animals--the donors of the plague pathogen--and the recipient animals.

The second form gives rise to a sluggish course of the epizootic process. In it, even during the period where sousliks are highly susceptible to the plague, the infectious process drags out somewhat, and in a number of cases the animals even recover; in the case of a fatal outcome of the disease it is not always associated with a well expressed bacteriemia. The frequency of intraspecies contacts with this form is lessened in connection with the slow motor activity of the hosts of the plague pathogen and the relatively slight active and passive movements of the fleas. Such a slow circulation of the plague pathogen is characteristic of the combination of semideserts, created in the Black Lands in the spring-summer. Thereby, intraspecies contact between individuals in souslik populations through the medium of the fleas is delayed.

In the presence of a number of favorable conditions active widely developed epizootics occurred in the former case in the focus; in the latter case, under the same conditions, quite often there were smoldering localized territorial epizootics.

The active epizootics were also observed in the il'men-delta region, characteristic of which, when the pathogen penetrates here, is a regular involvement of a number of species of rodents aside from the sousliks in the epizootics; jirds, mice, jerboas. As the result of the great activity of rodents the spread of the plague pathogen can occur very quickly in this area.

Observations made in the focus have shown that the spread of the epizootics proceed unequally in all directions in concentric circles, like the spread of a spot of oil on paper but only in the direction of those ecological grooves, where the motive forces can assure the development of an active epizootic process. These motive forces are chiefly a high census of the main or even secondary sources of the pathogen of the infectious disease and of the vectors. Thereby, evidently, two basic mechanisms operate which lead to the spread of plague. The first mechanism provides for the advance of the epizootic in a relay, that is, by the transmission of the pathogen through the medium of continuous contact of rodents with one another through their fleas. It is realized through the high degree of motor activity of the rodents and fleas even when the line of advance of the plague microbe may be quite limited spatially in each separate link of this transmission chain. Naturally, with this mechanism the rate of movement of the epizootic is determined chiefly by the degree of mobility of the rodents, which is very great in Yergeni, the Western Yergeni steppes and in the il'men-delta region, and considerably lower in the Black Lands.

The second mechanism is responsible for the transmission of the pathogen "in jumps". In this case the infected fleas negotiate considerable spaces by means of passive movement on hosts not characteristic of them and which, at the first opportunity, they attempt to leave. Possibly, by means of this mechanism specifically the plague pathogen has penetrated into the territory of Groznenskaya Oblast and the adjacent Black Land territory.

On the basis of all the information accumulated about the epizootic activity of the focus during the more than 40 years of study of it as well as in consideration of measures taken in the focus, its current history and the history of work in it can be arbitrarily divided into four main periods.

The first period includes the time from 1913 through 1924. During this period the fact of infection of dwarf

sousliks with plague was established, and it was noted that epizootics among them are repeated with relative constancy. These essentially were years when research work was developed on a small scale, because at that time the first World's War and then the Civil War occurred. After them followed a period of post-war ruin, during the course of which the main attention was paid to restoration of the economic life of the country.

The second period lasted from 1925 through 1932. During this period the network of plague institutions in the focus was expanded and was manned to a considerable degree. Study of the infectious nature of the focus became the subject of the principal activity of specialists in plague. In connection with this, it was possible to determine the fact that plague epizootics among rodents in the focus are repeated regularly from year to year. Thereby, active courses of these epizootics over tremendous spaces of the focus, particularly in Yergeni and in the West Yergeni steppes, were characteristic for many years. Then, the basic rules and regulations of plague epizootology among sousliks were demonstrated. Therefore, it is not by chance that toward the end of the second period a plan of operation was adopted directed at eliminating the plague pathogen from the focus by the method of "repeated solid" souslik elimination from its territories.

The third period lasted from 1933 through 1945. Characteristic of this period was a large volume of work on souslik extermination. In connection with this measure the infection in the focus very rapidly and sharply declined. However, the focus was not completely rid of the plague pathogen. Plague infection was maintained particularly in the eastern portion of the Black Lands, where extermination operations against sousliks were accomplished on a small volume and with inadequately good quality. Incidentally, it should be taken into consideration that during the Second World War and temporary occupation of the larger part of the territory of the Northwest Caspian Region by the enemy, prophylactic operations associated with rodent extermination were practically not carried out here.

Finally, the fourth period, which began in 1946 has lasted until the present time. During this period measures were taken directed at reinforcing the results of improvement of the focus which had been obtained on the territory of the larger part of the focus by extermination operations of the previous period. In this part of the focus plague epizootics among rodents could no longer be found. At the same time, in the eastern regions the infection had increased by this time, and plague epizootics began to be recorded on new territories,

which, on the one hand, led to the need for further study of the rules and regulations of the plague enzootic in these places, and, on the other, to taking a combination of prophylactic measures with the aim of complete suppression of the plague infection in the entire focus. During this period definitive concepts were gained about the opizootological inequality of different parts of the focus and their inequality from the viewpoint of the power of the enzootic factors.

As the result of extermination measures taken, lasting to the present time, the infection in the focus has been suppressed in the eastern portion of it. However, not enough time has gone by since the recent (1951 and 1954 in the Black Lands and 1956 in Dagestan) though very slow-moving epizootics; therefore, it is not yet possible to give any final judgment about the elimination of the plague pathogen from the entire territory of the focus in the Northwest Caspian Region.

Existential Conditions and Most Important Epizootological Characteristics of the Aral Area of the Central Asiatic Plain, Natural Focus of Plague

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The territory of the Aral region is included in the Central Asiatic Plain, natural focus of plague. It includes the subzone of the southern steppes, semidesert and northern desert, being equal to approximately 400,000 square kilometers in area. It is practically impossible to separate this territory from adjacent territories of the focus (central and southern Kyzyl-Kumy, Mangyshlak). In the north the boundary of it coincides with the common boundary of the natural central Asiatic plague focus.

Study of this territory has made it possible to divide it into the following twelve geographic regions (Fig 1): (1) the Aktyubinsk steppe region; (2-3) the Embinsk-Ural'sk and Sredne-Irgiz semidesert region; (4) Mugodzhary; (5) Irgiz-Turgaysk lake region; (6) the southwest border of the Kazakhskiy Melkosopochnik; (7) the mesa region of the northern Aral area proper (north shore of the Aral Sea with the adjacent areas); (8) the mosaic sandy area of the Aral portion of Kara-Kumy; (9) Predustyurt'ye; (10) northern Ustyurt; (11) northern Kyzyl-Kumy; and (12) the right bank of the middle course of the Syr-Dar' River (the Dar'yalyk-Takyr plain) with the lowlands of the Sarysu and Chu Rivers and the Arys'-Kumy sands. Each of these regions may be divided into even smaller natural areas. (Mention should be made of the tentative character of the territorial division presented. With further study of it the number of regions separated out undoubtedly should increase. In exactly the same way the boundaries of these regions can be determined only very schematically at present. This applies particularly to the northern regions which so far have been relatively very poorly studied.)

The geographic regions differ from one another not only in their flora and in their fauna but also in the composition of the reservoirs and vectors of the plague microbe and the nature of epizootics. Plague epizootics have been detected in four regions: on the north shore of the Aral Sea, in the Aral area of Kara-Kumy, on the right bank of the middle course of the Syr-Dar' River, and in northern Kyzyl-Kumy. In the northern part of the territory under analysis, that is, in the steppe and semidesert regions of Aktyubinskaya Oblast, Mugodzhary and the Irgiz-

Turgaysk lake region, there are no stable natural plague foci, apparently.

For the focus as a whole spontaneous infection of 10 species of rodents with plague has been established at the present time (great sand rat /Rhombomys opimus/, meridional jird /Meriones meridianus/, crested /Meriones tamariscinus/ and red-tailed /Meriones erythrourus/ jirds, dwarf /Citellus pygmaeus/ and Caspian /Citellus fulvus/ sousliks, the house mouse, gray hamster /Cricetulus migratorius/, alactaga /Alactaga jaculus/ and the jerboa Scirtopoda telum; also spontaneously infected are two species of carnivores (Siberian polecat /Mustela eversmanni/ and weasel), 10 species of fleas (Xenopsylla skrjabini, X. gerbilli caspica, Ceratophyllus laeviceps, C. tesquorum, C. aralis, Coptopsylla lamellifer, Oropsylla ilovaiskii, Ctenophthalmus dolichus, Stenoponia conspecta, Rhadinopsylla cedestis), and two species of ticks (of the genera Haemaphysalis and Hyalomma).

The total number of plague microbe cultures isolated during investigations from 1945 through 1956 reaches 1040. Of this number 773 were isolated from the animals and 267 strains from ectoparasites. The relative frequency of isolation of cultures from different species of animals and their ectoparasites is seen from Table 1 and Figs 2 and 3.

Table 1

Number of Plague Microbe Cultures Isolated from Different Species of Rodents and Carnivores in the Northern Aral Area in 1945-1956

1 Вид животного	2 Март-июнь		3 Июль-ноябрь		4 Всего	
	5 исследовано зверьков	6 выделено культур	5 исследовано зверьков	6 выделено культур	5 исследовано зверьков	6 выделено культур
7 Большая песчанка	86807	198	162619	458	249426	656
8 Полуденная песчанка	4407	4	10382	17	14789	21
9 Краснохвостая песчанка	3608	2	4133	5	7741	7
10 Гребенщиковая песчанка	2614	—	3611	2	6225	2
11 Малый суслик	76364	41	4057	2	80421	43
12 Желтый суслик	18381	26	68	—	18449	26
13 Домовая мышь	19872	—	15577	11	35449	11
14 Серый хомячок	737	1	221	1	958	2
15 Большой тушканчик	937	2	162	—	1099	2
16 Емуранчик	1246	—	161	1	1407	1
17 Степной хорь	510	—	519	1	1029	1
18 Ласка	67	1	73	—	140	1
19 Итого	215550	275	201583	498	417133	773

1. species of animal; 2. March-June; 3. July-November; 4. total; 5. animals investigated; 6. cultures isolated; 7. great sand rat; 8. meridional jird; 9. red-tailed jird; 10. crested jird; 11. dwarf souslik; 12. Caspian souslik; 13. house mouse; 14. gray hamster; 15. alactaga; 16. Scirtopoda telum, jerboa; 17. Siberian polecat; 18. weasel; 19. total.

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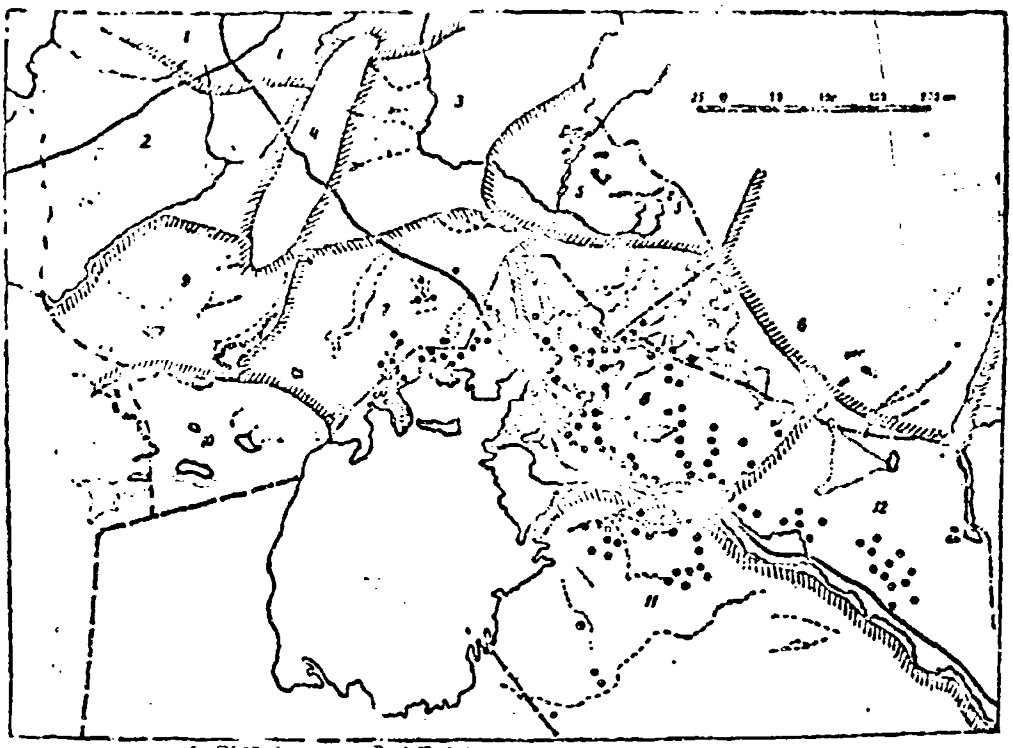

Fig 1

Natural Regions of the Northern Aral Area

1. southern steppes; 2. desert steppes; 3. Mugodzhary; 4. Irgiz-Turgaysk lake region; 5. Kazakhskiy Melkosopochnik; 6. mesa region of the north shore; 7. Aral area of Kara-Kumy; 8. Predustyurt'ye; 9. north Ustyurt; 10. north Kyzyl-Kumy; 11. right bank of the middle course of the Syr-Da' River. The black circles represent "epizootic points".

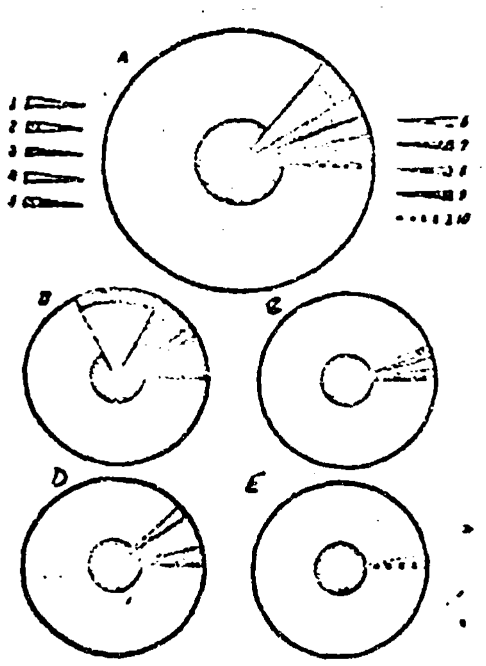

Fig 2

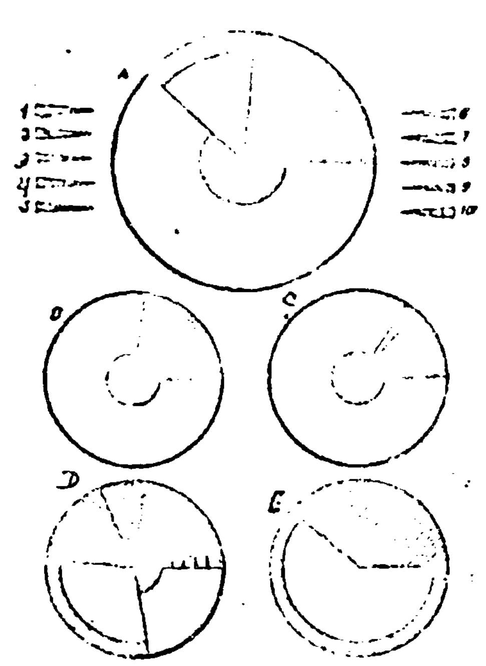

Fig 3

Percentage of Plague Microbe Cultures Isolated from Various Species of Mammals in the Northern Aral Region. A. all of the north Aral Region; B. north shore; C. Aral portion of Kara-Kumy; D. right bank of the middle course of Syr-Dar' River; E. northern Kyzyl-Kumy. 1. great sand rat; 2. dwarf souslik; 3. Caspian souslik; 4. meridional jird; 5. crested jird; 6. red-tailed jird; 7. gray hamster; 8. house mouse; 9. jerboas (Alactaga and Scirtopoda telum); 10. carnivores (Siberian polecat and weasel).

Degree of Infection of Various Species of Fleas During Plague Epizootics in the Northern Aral Region. A-E--see explanations to Fig 2; 1. Xenopsylla Skrjabini; 2. X. gerbilli caspica; 3. Ceratophyllus laeviceps; 4. C. tesquorum; 5. Oropsylla ilovaiskii; 6. Coptopsylla lamellifer; 7. Ctenophthalmus dolichus; 8. Stenoponia conspecta; 9. Rhadinopsylla cedestis; 10. Ceratophyllus aralis.

Everywhere, great sand rats and their fleas occupy a predominant position among the reservoirs of plague in the northern Aral region. From them 85 and 97 percent of all the strains obtained, respectively, have been isolated. On the north shore of the Aral Sea dwarf sousliks have participated notably in the epizootics in various years (1946, 1948), and in the region of the lower course of the Syr-Dar' River and partly on the north shore of the seaCaspian sousliks have participated.

The individual regions of the focus are different in an epizootological respect. These differences concern both participation of different species of rodents and ectoparasites in the epizootics and the comparative epizootological significance of various species as well as the seasonality of the epizootics, the nature of their courses and the effect of epizootics on the rodent census.

On the north shore of the sea and in the adjacent regions the species range of mammals involved in the epizootic is distinguished by the greatest variety (Fig 2). Here, participation of 10 species of rodents and one species of carnivore (the Siberian polecat) has been recorded in the epizootics. In second place after the great sand rats, from which 66.8 percent of all the plague microbe cultures are obtained here, are (although not every year) dwarf sousliks. In this region, during the period from 1945 through 1950, 35.8 percent of the cultures (38 out of 106) were obtained if we consider only cultures isolated from rodents in the spring-summer season, or 16.2 percent of the total number of cultures, equal to 241 for this region. From Caspian sousliks in this region 6.7 percent of the total number of cultures were isolated. The other species of rodents were involved in the epizootic only in isolated cases, although repeatedly: the meridional jird, in 1945, 1946 and 1947; the red-tailed jird, in 1946, 1948 and 1949; the crested jird, in 1945 and 1947; the gray hamster, in 1946, etc. An exception is constituted only by the relatively mass participation of house mice in the autumn epizootic of 1947. Only a single culture (1950) was obtained from the Siberian polecat in all these years.

In the Aral portion of Kara-Kumy seven species of rodents were recorded as participating in the epizootics in 1947-1956, while on the territory of the right bank of the middle course of the Syr-Dar' River (1947-1951 and 1955-1956 epizootics) only five species were recorded. In the first of these two regions, aside from great sand rats from which 93.3 percent of the cultures were obtained here, only meridional jirds were involved in the epizootic to a quite notable degree (2.2 percent of the cultures in 1947, 1955 and 1956) as well as Caspian sousliks and red-tailed jirds (respectively 1.6 percent of the cultures in 1948-1950, 1953 and 1956, and 1.4 percent of the cultures in 1950-1951 and 1954). In the second region, aside from great sand rats (87.6 percent of all the cultures were obtained from them) apparently the meridional jirds (6.8 percent of the cultures during the 1950 and 1955-1956 epizootics) were involved in the epizootics and not by chance.

In northern Kyzyl-Kumy plague cultures were isolated almost entirely from great sand rats in 1951 and from 1953 through 1956 unless

we take into consideration a single strain obtained from a meridional jird and one from a weasel (Fig 2).

The same may be said with respect to differences in the infection of rodent fleas with plague in these regions (Fig 3). This picture may be partly the result of different degrees of study of the various regions. However, it is beyond doubt that in large measure it reflects actual differences in plague epizootology in these regions.

The very important epizootological significance of the great sand rat in the focus, aside from its mass distribution, being the main species here, is explained not so much by its susceptibility to the infection as by the nature of its colonies and the arrangement of its complicated colony-holes. As has been shown by Ya. P. Vlasov (1937), M. V. Shekhanov (1952), K. T. Krylova, S. N. Varshavskiy, Ye. S. Shilova, M. N. Shilov and G. I. Podlesskiy (1957) great sand rat colonies serve as habitats for a complex interrelated society of sand rat neighbors—warm blooded and cold blooded animals, including reservoirs and vectors of the plague pathogen. Colonies of great sand rats in the Aral region constitute places in which provision is made for natural multiplication and constant preservation of the plague microbe.

This fact caused us to direct concentrated attention to the clarification of details of the distribution of great sand rats and the characteristics of their colonies.

As a result of many years of study three main types of great sand rat colonies were distinguished: continuous or uniform, band-like and combined, and insular. The first type of sand rat colony is encountered in the Aral region in the large sand areas (southern sweep of Bol'shiye Barsuki, various areas of the Aral region of Kara-Kumy, and northern Kyzyl-Kumy) and in the plakor type of locality /a plakor is an elevated plain region, the soils and vegetation of which most fully express the zonal features of the landscape of a given zone/ of the Ustyurt plateau. As has already been pointed out by N. P. Naumov (1954a, 1954b), it is characterized almost always by a high population density, uniform distribution of the colonies and, as a rule, by the absence of local accumulations of them. The great sand rat colonies in the sands are distinguished by their comparatively large size. As a result of a relatively large reserve of colonies in the settlements, a considerable percentage of them not uncommonly is vacant. As the observations of I. L. Kulik have shown (1954, 1955, 1956), made on labeled sand rats in these settlements in northern Kyzyl-Kumy, the animals come here first for multiplication, frequently change holes, resettling even with small hairless offspring, and are in frequent contact with one another. At the same time, it should be noted that in many of the continuous sand rat settlements, particularly in the northern Kyzyl-Kumy, there are fewer ectoparasites (Naumov, 1954a; Varshavskiy, 1955a, 1956b) and cohabitants from groups of other species of sand rats /jirds/, jerboas and other rodents are more infrequent.

The band and insular settlements, differing in a number of essential characteristics, have at the same time much in common with each other. They are due either to erosive clefts (the band settlements in

clayey desert, in the valleys of the north shore of the sea and in Produstyurt'ye) or to a combined landscape in which islets or mounds of sand alternate with clayey takyr-like areas [takyrs are clayey or heavy sandy loam desert soil with hard and smooth surfaces broken up into multiple units by cracks] (insular settlements in some regions of northern Kyzyl-Kumy and the right bank of the middle course of the Syr-Dar River). In these settlements the colonies, as a rule, are small in size, are unequally distributed and form local accumulations. The average population density of the animals here, as calculated with respect to the entire area rather than simply for places inhabited by sand rats, is frequently several times less than in the continuous settlements. The number of colonies per animal is usually less also, for which reason the sand rats are much more attached to definite colonies in the non-uniform settlements. Apparently, in a number of cases, we may even speak of a relative shortage of shelters in these types of settlements, which explains the rapid settlement of colonies which for any reason have lost their inhabitants. The food supply for the great sand rats in the insular settlements is usually poorer than in the adjacent sands, and according to the observations of I. L. Kulik (1955, 1956), they begin multiplication under these conditions after almost half a month's delay. In the band settlements movement of the animals is accomplished along the settlements. Therefore, here there are more or less well-defined "migration roads", which are absent from the continuous settlements (Shekhanov, 1952; Naumov, 1954a). Finally, the sand rat holes in the non-uniform (band and insular) settlements are used actively not only by the hosts themselves but also by various warm blooded cohabitants, and infection of the rodents with ectoparasites in such settlements, for example, in northern Kyzyl-Kumy (Darskaya, 1955b) is much higher than in the neighboring continuous settlements.

Various types of settlements of great sand rats are different in the nature of changes in the census of the animals. In the band settlements it, as a rule, is relatively constant and does not undergo any prolonged or deep-seated depressions, including large areas. This is evidenced by the results of many years of methodical observations of the census of great sand rats in the dry valleys of the north shore of the Aral Sea since 1947.

From Table 2 and Fig 4 it is clearly seen that in the band settlements of great sand rats the habitation of colonies, although it undergoes considerable seasonal variations, almost always increases quite rapidly, even after a sharp drop produced by unfavorable conditions.

Thus, in Kiyaksay valley the habitation of the colonies, after a sharp drop in the winter of 1948/49 and 1953/54, returned to a quite high level as early as the autumn of 1949 and 1954, respectively. In the valleys of Baykun, Chokusu and Turangly the habitation of the colonies, very markedly reduced for several winter and spring seasons (in the latter case, they were flooded with thaw water), not uncommonly increased considerably as early as the autumn season of the same year.

Table 2

Changes in the Habitation of Colonies in the Band and Continuous Settlements of Great Sand Rats in Different Years

Название урочища	Сезон	Обитаемых колоний в разные годы 1947	1948	1949	1950	1951	1952	1953	1954	1955	1956	1957
Ленточные поселения												
Маргенсай	весна	—	53,6	61,5	37,5	78,9	71,9	59,4	63,4	85,9	52,1	76,5
	осень	90,0	93,0	95,8	93,3	92,4	89,7	83,7	91,0	85,0	91,6	91,7
Кияксай	весна	—	85,7	43,8	57,2	50,0	66,7	57,4	49,1	71,2	72,7	85,7
	осень	91,1	94,1	84,0	83,3	66,7	86,5	87,0	85,2	86,9	92,3	100,0
Чокусу	весна . .	—	41,7	33,7	44,4	56,6	23,9	24,5	10,6	23,3	25,7	54,1
	осень . .	81,7	93,3	82,9	90,7	61,9	55,0	61,9	17,5	46,5	58,5	84,0
Саралжинсай	весна . .	—	44,4	83,3	80,0	34,6	33,6	60,0	31,3	67,0	20,9	88,6
	осень . .	66,4	83,7	94,1	83,8	38,1	73,7	80,0	65,5	80,7	93,9	92,0
Байкун	весна . .	—	57,5	50,0	20,0	35,7	42,8	7,3	26,9	—	77,8	84,1
	осень . .	—	71,4	86,7	71,6	54,4	55,5	40,8	69,2	64,3	90,5	80,6
Тураигль (восточная)	весна . .	—	52,0	14,3	33,3	54,3	39,5	27,3	23.3	—	60,7	59,7
	осень	—	61,9	65,0	53,2	63,7	52,6	69,0	41,9	63,0	81,8	66,7
Ак-Кудук	весна	—	80,0	66,6	73.9	57,9	21,1	31,3	72,8	75,3	50,0	62,7
	осень	—	92,7	90,9	75,0	97,5	59,5	89,5	75,0	73,5	88,7	95,4
Сплошные поселения												
Чет-Кудук	весна	—	83,3	53,3	80,0	23,5	37,2	39,3	28.1	86,2	7,4	37,7
	осень	92,5	95,5	96,1	96,9	31,5	50,2	91,6	54,1	16,7	66,5	90,9
Якши-Клыч	весна . .	—	—	37,5	79,2	73,8	24,0	59,0	59,6	38,1	78,2	25,5
	осень . .	—	96,3	93,7	69,8	86,5	76,6	87,9	—	—	53,3	86,5
Куланды	весна . .	—	62,0	1,5	0	0	8,9	44,0	77,1	61,0	55,3	71,0
	осень . .	84,0	2,3	2,1	—	0	54,0	90,0	67,5	70,0	100,0	100,0
Чегонак	весна	—	—	0	0	7,1	17,9	53,2	45,0	65.0	24,6	70,8
	осень	98,0	3,3	—	—	1,3	72,2	77,7	100,0	41,3	81,6	90,0

Notes: natural landmarks 1-6 are located in the dry valleys of the north shore of the sea; natural landmark 7, in a belt near the sea; landmarks 8 and 9, along the extent of the sands in the Aral portion of Kara-Kumy; landmarks 10 and 11, along the extent of sands on the north shore of the sea. 1. name of natural landmark; 2. season; 3. percent of colonies inhabited in different years; 4. band settlements; 5. Margensay; 6. Kiyaksay; 7. Chokusu; 8. Saralzhinsay; 9. Baykun; 10. Turangly (eastern); 11. Ak-Kuduk; 12. continuous settlements; 13. Chet-Kuduk; 14. Yakshi-Klych; 15. Kulandy; 16. Chegonak; 17. spring; 18. autumn.

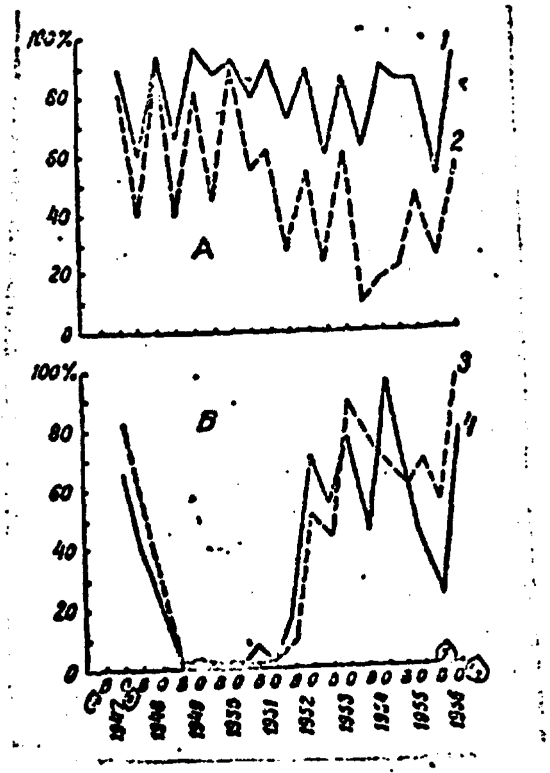

Fig 4

Changes in the habitation of colonies of great sand rats in different types of settlements. A. band settlements (dry valleys); B. continuous settlements (sand areas): 1. Margensay; 2. Chokusu; 3. Chegonak; 4. Kulandy; 5. spring; 6. autumn.

On the other hand, the number of animals in the continuous settlements and the habitation of colonies in them vary a great deal more. It is important to note that characteristic of these settlements are deep and long drops in the census which not uncommonly extend over considerable areas. Existing data indicate the fact that under such conditions reduction of the great sand rat population not uncommonly occurs to such a great degree and sometimes over such extensive spaces that subsequent recovery of the rodent census occurs slowly, dragging on for a number of years.

Thus, after the mass extinction of great sand rats in the plakor type of terrain in north Ustyurt, which apparently occurred before 1948, because in the summer of that year only isolated colonies settled here, the population census of sand rats remained at a very low level

for several years; the habitation of the colonies did not exceed 20 percent and began to rise notably only in 1953, that is, after five years. In exactly the same way, after extinction of great sand rats in the first half of 1948 in the region of the north shore of the sea adjacent to the southern ends of the Bol'shiye Barsuki sands, where in the autumn of 1948 and the spring of 1949 no more than 0.5 percent of the colonies were inhabited, extremely low habitation figures for the settlements were observed for four years. Only in the autumn of 1952 did settlement of the colonies by the great sand rats reach 54.0-72.2 percent, although even in the spring of that year it did not go higher in various places than 8.8-17.9 percent. Similar observations have been made in the northern part of Kyzyl-Kumy.

On some areas the census of great sand rats is particularly constant. Even in the case of profound and extensive drops in the census, foci with a relatively abundant population of the animals are usually maintained in these areas. Such areas deserve the name of "habitation areas" or "survival foci" of the great sand rats. Against the background of a general drop in the census these areas were found along the margins of the sand massifs, along the borders of the ancient and modern Syr'-Dar' valleys, at the point of junction of the ancient valley and the plateau, along the railroad bed and along the overland roads. Such survival areas in general coincide with those areas of contact between different landscapes where the complex local terrain and the mosaic vegetation assure particularly favorable existential conditions for the great sand rats.

From what has been presented it is easy to see that the conditions of distribution and preservation of the plague microbe in various sand rat settlements differ. Penetration of the pathogen into continuous settlements can be associated with extensive distribution of it and extinction of the animals with subsequent drop in their census. Epizootics thereby do not have to be plague epizootics. However, whatever they are, they make it impossible for the plague pathogen to be maintained constantly in such settlements.

In the band and insular settlements there are practically no conditions for the spread of acute diffuse epizootics, which is in good correlation with the relative stability of the census observed here. This stability, like the abundance of cohabitants, contributes to establishment of the plague pathogen. We shall return to these problems below.

A most important regulation of the course of plague epizootics in the north Aral region may be considered their biphasic nature, produced by adaptation to definite seasons. For the Aral region such rules and regulations have already been noted by A. A. Zuchayev and S. N. Varshavskiy (1952). It is apparently a common feature for all the desert foci. The development of epizootics among the animals is observed in the spring and in the early summertime (April-May-June) and, on an even greater scale, in the autumn, in September-October (Fig 5).

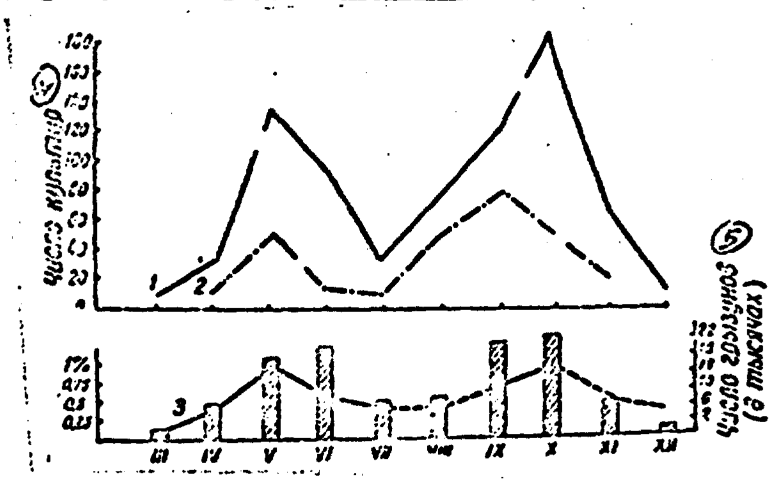

Fig 5

Seasonality of plague epizootics in the north Aral region. 1 number of cultures from rodents; 2. number of cultures from ectoparasites; 3. percent of rodents infected; the columns indicate the number of rodents investigated. 4. number of cultures; 5. number of rodents (in thousands).

This seasonality of the development of epizootics is associated chiefly with the increase in the census of the animals in those seasons as a result of their multiplication, production of ectoparasites, increase in the mobility of the sand rats and of their cohabitants and increase in the contact of animals with infected holes. The cases begin in the spring after the redistribution of hibernating animals and reach a maximum during the period of multiplication and subsequent dispersal and settlement of the young portion of the population. The autumn rise in morbidity is favored by the predominance of young animals, which are more susceptible to the infection, in the settlement as well as by the particularly marked increase in contact during the period of active storing of food and pre-winter reconstruction of the dwellings. Apparently, changes in the susceptibility of the animals and in the census of the leading species of fleas as well as other conditions which have not yet been studied well are of importance for the seasonality of the epizootics.

Disturbances of the seasonality of epizootic development are associated with an unusual course of general seasonal phenomena in the Aral region. Thus, an increase in the epizootics in the summer months was noted in August 1953 and 1954 in the central part of the Aral portion of Kara-Kumy and in July-August 1946 and 1947 in the western part of the north shore of the sea. The slight development of the autumn morbidity of the rodents was observed in 1946 in the western and in 1948 in the

eastern part of the north shore, while in the very dry years, 1951 and 1955, in the Aral portion of Kara-Kumy as well. These characteristic features were preceded either by an increase in the number of cases in the summer or by a low spring multiplication of the animals.

The characteristics of seasonal development of epizootics in various natural regions of the focus have not been studied well yet. On the north shore of the sea, in connection with the notable participation of sousliks in the epizootics, the spring peak in the morbidity is not uncommonly equal to the autumn peak or even higher than it. In the southern regions the autumn peak in the development of the epizootic wave is acquiring progressively greater significance.

Characteristic of the Aral region and part of the central Asiatic focus are the alternation of periods with acute and slow-moving epizootics as well as the existence of places in which the plague pathogen is found for a long time (several years straight). These are the so-called "elementary" foci, about which we will speak in greater detail below.

The nature of the epizootics does not remain constant and is related to the census and mobility of the rodents. The former is connected with weather conditions of the previous years, whereas the mobility is conditioned chiefly by the meteorological circumstances of the given year. Both are responsible for the degree and intensity of intra and interspecies contact.

The most acute and most widespread epizootics were observed in the northern portion of the Aral region in the presence of a high census of the main species of rodents, particularly after successful multiplication and survival of them in previous favorable years. They were noted in years with a dry spring and summer, at which time there was a marked increase in mobility (contact) of the rodents and where the physiological resistance of the animals to diseases decreased because of a shortage of food. The 1947 and 1948 epizootics, recorded at scores of geographic points, were of this type. In various cases a study was made of the successive spread of the epizootics in the band settlements and the passage of it into continuous settlements of the great sand rats. Of a similar nature were the extensive epizootics of 1953 and 1954 in the Aral portion of Kara-Kumy and northern Kyzyl-Kumy. In the extremely dry year, 1955, the epizootic included also the right bank of the middle course of the Syr'-Dar' River in addition to these two regions.

During these epizootics an increased infection of ectoparasites was recorded, from which, as a rule, a considerably larger percentage of cultures was isolated than in the other years. Thus, in 1947 and 1948, during an investigation made chiefly of fleas taken from the animals themselves, 39 strains of the plague microbe were isolated, that is, 12 percent of the total number of strains, equal to 323. In 1953-1955, when the greatest attention was given to investigating fleas taken from the entrances to the holes of the great sand rats this percentage increased to 40 (180 cultures out of 442). During years without acute or extensive epizootics (1949, 1951, 1952, 1956) it was low (21 strains out of 155, or 13.5 percent), which apparently is evidence of the secon-

dary significance of fleas in prolonged preservation of the plague pathogen in the Aral focus.

Acute epizootics died down with a drop in the rodent census and with a reduction in their mobility. The latter was usually due to favorable weather, chiefly to adequate moisture and associated good yield of food. Improvement of the physiological conditions of the animals corresponded with a reduction in mobility. Characteristic in this respect are the moist years, 1949 and 1956, when only small focal epizootics were observed which did not show any inclination to spread to adjacent areas.

The rules and regulations established are important in practice, because they can serve as the biological basis for prognosis of the epizootological situation. It should be added that for successful epizootological prognosis observations and predictions of changes in the censuses of the rodents themselves, particularly of great sand rats, red-tailed jirds and meridional jirds and sousliks are also necessary, as well as a clarification of the degree to which conditions favor their existence, chiefly changes in the availability and quantity of food of a definite quality. In the deserts these changes depend chiefly on the degree and distribution of precipitation, whereby in the Aral region usually precipitation and the temperature are of the greatest importance for the yield of food in the spring. Considerable snowfall in the winter in the absence of spring precipitation has a favorable effect on the development of vegetation only in the warm spring, when the thaw water is to a considerable degree absorbed by the soil and the temperature conditions favor early vegetation of plants. As far as determinations of the status of great sand rat populations are concerned, experience which has been accumulated in the Aral region constitutes evidence to the effect that the degree of settlement of the colonies, average number and composition of animals living there, the course and rates of multiplication serve as good indications of both the total census of the population itself and of the conditions favoring its existence (Varshavskiy and Shilov, 1955, 1957).

The elimination of infectious diseases from the territories following acute and widespread epizootics occurs in a different manner in its various portions.

After claims were rejected about "transformations" of the plague microbe to a form undetectable by ordinary methods and back to the visual form, the main condition for its permanent existence in nature in a virulent form must be considered the adequate frequency of passage through susceptible rodents and fleas, which can be assured only by the necessary frequency of their contact. Therefore, the problem acquires chiefly an ecological character and, aside from study of the dynamics of susceptibility of warm-blooded animals and the behavior of the microbe in fleas, it amounts to elucidation of the mechanisms of contact of rodents with one another or changes in their census and mobility in connection with environmental conditions.

Only in a few places are the conditions combined so that actually and for practical purposes continuous reproduction of the plague microbe

occurs. In such places, in elementary foci or in areas of survival the plague microbe lives constantly, whereas in all other areas it can only be a temporary guest. As has been shown above, only the non-uniform (band or insular) settlements possess conditions for such a stable preservation of the pathogen.

Ten years of observations in the Aral region, in our viewpoint, showed quite convincingly the existence of elementary foci of plague infection in such settlements. On the north shore of the Aral Sea and the region of the Kara-Tyuba peninsula preservation of the plague microbe was observed on localized areas no more than ten square meters in area for three years—from 1945 through 1947 inclusive. Such areas were the lowlands of the dry Daulen valley (the Ashchekuduk natural landmark), the lowlands of the Soleuly, Kirey valleys, the natural landmark of the Kobugor and Ashchekuduk valley. In the last two years here single cultures were isolated in the absence of cases among rodents in adjacent areas, which were investigated just as carefully (Fig 6).

In the northwestern part of the Aral portion of Kara-Kumy six such elementary foci were found. Thus, in the Chet-Kuduk natural landmark the plague microbe was found every year from 1947 through 1950; in the Yakshiklych landmark, from 1947 through 1949;and in 1952 in three elementary foci (the Mayman natural landmark, Karagul' and the environs of the railroad siding No 83) infected rodents were found in the same years, missing one or two years, and in the Kaydaul natural landmark they were found in 1953, 1954 and 1955.

Along the western and southern margins of the Aral area of Kara-Kumy adjacent to the railroad strip seven areas were found in which the plague microbe was preserved for a long time. At one point (Khanturtkul') the plague pathogen was recorded in 1953 and 1955; in another (the environs of Kamyshlybash station), in 1953, 1954 and 1955. At two points (the environs of Chumysh station and siding No 92) it was found from 1952 through 1954 and in 1955. In the environs of railroad siding No 98 plague was recorded in 1950, 1951, 1953, 1954 and 1955. Near Maylibash station and Baykhozh cultures of the plague microbe were isolated in 1947 and then from 1950 through 1956 inclusive, that is, for 10 years with 1- 2- year interruptions at various points. Finally, near the Dzhusaly station in the Sukhoy Aryk natural landmark and in the 40th kilometer of Novo-Karakumskaya highway plague was recorded for three years straight (respectively, in 1947-1949 and 1948-1950), and between the 70th and 76th kilometers it was found on the old Karakumskaya highway in 1948, 1950 and 1956 (Table 3).

In all these cases the plague microbe was isolated repeatedly from rodents or much less commonly from fleas caught on a small territory with an area, usually no more than 10-15 square kilometers, approximately unitypical in a landscape respect. A considerable part of the cultures was isolated in the elementary foci in the so-called "inter-epizootic" periods when no cases of disease were noted in the rodents in the adjacent areas. Finally, these cultures were single findings, almost always separated from one another by considerable periods of time.

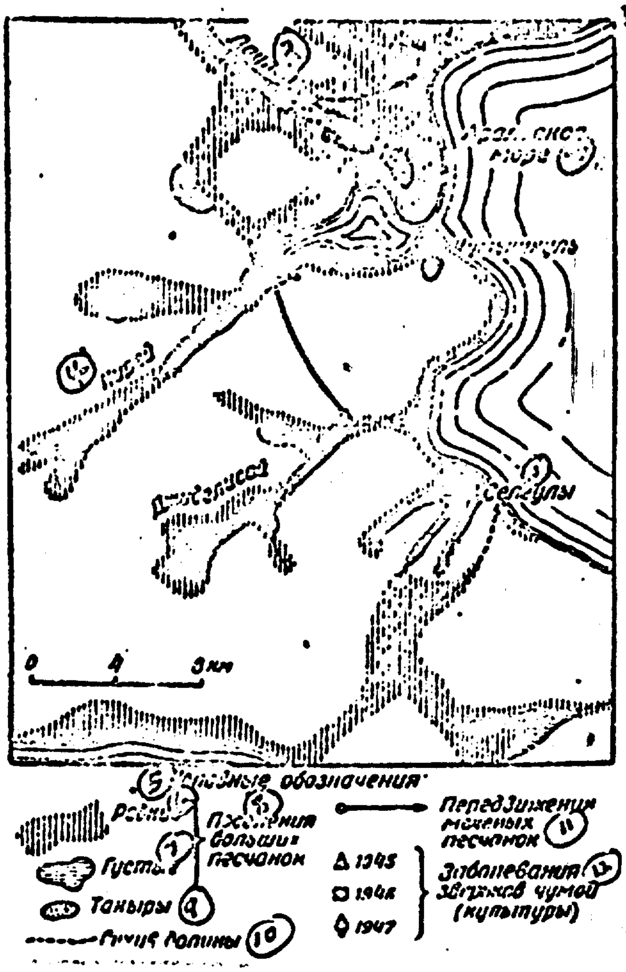

Fig 6

Elementary plague foci in the north of the Kara-Tyuba peninsula (settlements of great sand rats, migrations of labeled individuals and places at which plague microbe cultures were isolated from the animals and fleas in different years). Three areas are easily distinguished, where the plague microbe was found for three years straight (the lowlands of the Daulen, Kirey and Seleuly valleys). 1. Seleuly; 2. Aral Sea; 3. Daulen; 4. Kirey; 5. key: 6. infrequent; 7. dense; 8. settlements of great sand rats; 9. takyrs; 10. dry valleys; 11. migrations of labeled sand rats; 12. cases of plague among the animals (cultures).

Table 3

Elementary Plague Foci in the Northern Aral Region

1 Район	2 Местоположение элементарных очагов (колодец, урочище и т. п)	3 Число сезонов выявления чумного микроба в очаге	4 Сроки повторного выявления чумного микроба (сезон, год) в элементарном очаге	5 Примечание
6 Северное побережье Аральского моря (п-ов Кара-Тюб)	Ашекулук	3	осень 1945, 1946 и 1947 гг.	В 1946 и 1949 гг. проведены работы по истреблению грызунов
	Селеулы	3	осень 1945 г., начало лета 1946 г., осень 1947 г.	
	Низовья долины Кирей	2	осень 1946 и 1947 гг.	
	Кобуrор	2	осень 1946 и 1947 гг.	
7 Северо-запад Приаральских Кара-Кумов	Четкудук	5	осень 1947 г., лето 1948, весна и осень 1949, осень 1950.	
	Якшиклыч	4	осень 1947, 1948, 1949 и 1952 гг.	То же, в 1949-1950 гг.
	Майкак	2	осень 1947 и 1950 г.	
	Карагуль (окр. колхоза им. Энгельса)	3	осень 1947 г., лето 1948 г., осень 1950 г.	
	Кайдаул (Адраспан..дук, Джиланды)	4	лето 1953 г., весна и лето 1954 г., весна 1955 г.	То же, в 1954-1955 гг.
	Окр. разъезда № 83	2	осень 1947 и 1950 гг.	То же, в 1948-1950 гг.
8 Западная окраина Приаральских Кара-Кумов	Хангурткуль (Канртам)	4	весна и осень 1953 и 1955 гг.	
	Окр. ст. Чумыш	4	нач. лета 1952 г., весна 1953 г., начало лета и осень 1954 г.	То же, в 1953-1955 гг.
	Окр. разъезда № 92	3	весна 1952 г., осень 1954 и 1955 гг.	
	Окр. ст. Камышлыбаш	3	осень 1953 г., весна 1954 г., осень 1955 г.	
9 Южная окраина Приаральских Кара-Кумов	Район ст. Майлибаш	6	осень 1947 и 1950 гг., весна и лето 1951 г. весна 1952 г., осень 1953 г.	То же, в 1949, 1950 и 1955 гг.
	Район ст. Байхожа	5	осень 1947 г., весна 1950 г., осень 1954 и весна 1955 и 1956 гг.	
	Окр. разъезда № 93	6	осень 1950 г., весна 1951 и 1953 гг., осень 1953 г., весна 1954 и 1955 гг.	То же, в 1949, 1950 и 1955 гг.
10 Восточная окраина Приаральских Кара-Кумов	70-75-й км Старо-Каракумской дороги	3	лето 1948 г., осень 1950 г., лето 1956 г.	Истребление грызунов не провод.
	40-й км Ново-Каракумской дор.	3	осень 1948 г., весна 1949 г., осень 1950 г.	
	Сухой Арык (окр. Джусалов)	3	осень 1947 г., весна 1948 и 1949 гг.	Пров. истреб. грызун. в 1947-1949 гг.
11 Южная окраина равнины Дарьялык-Такыр	80-й км грунтовой дороги Джусалы — Кзыл-Орда	3	весна 1948 г., весна и осень 1950 г.	Истреб. раб. проведены в 1947, 1948 и 1950 гг.
	50-й км той же дороги	3	осень 1947 г., весна и осень 1948 г.	

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1. region; 2. location of elementary foci (wells, natural boundaries, etc.); 3. number of seasons plague microbe detected in the focus; 4. time of repeated detection of plague microbe (season, year) in elementary focus; 5. comment; 6. north shore of the Aral Sea (Kara-Tyuba peninsula); 7. northwest Aral region of Kara-Kumy; 8. western boundary of the Aral portion of Kara-Kumy; 9. southern boundary of the same; 10. eastern boundary of the same; 11. southern margin of the Dar'yalyk-Takyr plain; 12. Ashchekuduk; 13. Seleuly; 14. lowlands of the Kirey valley; 15. Kobugor; 16. Chet-Kuduk; 17. Yakshiklych; 18. Mayman; 19. Karagul' (environs of the Kolkhoz imeni Engel's); 20. Kaydaul (Adraspankuduk, Dzhilandy); 21. environs of railroad siding No 83; 22. Khanturtkul' (Kairtam); 23. environs of Chumysh station; 24. environs of railroad siding No 92; 25. environs of Kamyshlybash station; 26. region of Maylibash station; 27. region of Baykhozh station; 28. environs of railroad siding No 98; 29. 70th-76th kilometer of the Staro-Karakumskaya Highway ["staro" means old]; 30. 40th kilometer of the Novo-Karakumskaya Highway; 31. Sukhoy Aryk (environs of Dzhusaly); 32. 80th kilometer of the overland highway between Dzhusaly to Kzyl-Orda; 33. 50th kilometer on the same road; 34. autumn of 1945, 1946 and 1947; 35. autumn 1945, beginning of summer 1946, and autumn of 1947; 36. autumn 1946 and 1947; 37. autumn 1947, summer 1948, spring and autumn 1949, autumn 1950; 38. autumn 1947, 1948, 1949 and 1952; 39. autumn 1947 and 1950; 40. autumn 1947, summer 1948, autumn 1950; 41. summer 1953, spring and summer 1954, spring 1955; 42. autumn 1947 and 1950; 43. and ["B" and "O" mean "spring" and "autumn", respectively; for convenience these words will not be repeated; "S" means "summer"]; 44. beginning of the summer 1952, spring of 1953, and beginning of summer and autumn 1954; 45. in 1946 and 1949 rodent extermination operations were conducted here; 46. same in 1949-50; 47. same in 1954-1955; 48. same in 1948-1950; 49. same in 1953-1955; 50. same in 1949, 1950 and 1955; 51. same in 1949, 1950 and 1955; 52. no rodent extermination carried out; 53. rodent extermination conducted in 1947-1949; 54. rodent extermination operations in 1947, 1948 and 1950.

Usually, they occurred in the autumn, at a time when the rodent census reaches its yearly maximum and when there is an increase in the frequency of contact between these animals. Thus, of the total number of cases in which plague was found in the elementary foci, 57 percent occurs in the autumn, 30 percent in the spring, and 13 percent in the summer. In the northern half of the focus, the autumn emphasis is particularly distinct because there in the autumn 73 percent of the cases occur, while only 10 percent occur in the spring. On the other hand, in the southern half of the focus the incidence of spring and autumn plague detection is almost the same, 43 and 46 percent respectively, whereas in the summer only 11 percent of the cultures are found.

It should be noted that cultures isolated in the elementary foci, like cultures obtained during the acute epizootics, unfortunately were not studied, and nothing can be said about their characteristics. Individual observations have shown that along with the altered strains, the main mass is constituted by virulent strains of the plague microbe with a more or less typical morphology.

The facts presented show that in the Aral region the plague microbe exists in two alternating ecological forms (epizootological forms)—in the form of acute epizootics which represent mass multiplications of the plague microbe and in the form of enzootics which replace the epizootics when there is a reduction in the census of the reservoirs and vectors and increase in their resistance to infection and multiplication of the bacteriophage. (The authors have made an error in terminology. The idea about "ecological forms" of plague microbe which alternately make up its population contradicts what is known about ecological types from ecology. The concept "enzootic" is practically equivalent to the concept "natural focalization", that is, it includes all the conditions and manifestations of the infectious pathogen in the natural focus: both active epizootics and sporadic cases among reservoirs in the interepizootic seasons and years in which there are no epizootics. In presenting the interesting viewpoint of the authors it would have been more correct to say that the plague microbe is preserved in the deserts of the northern Aral region because of the alternation of two enzootic mechanisms—active diffuse epizootics and sporadic cases among rodents replacing them in the elementary foci or that the alternation of conditions of a relatively low census and mass multiplication are characteristic of the plague microbe in the natural focus (Editors)). The epizootics represent not only mass multiplications of the plague pathogen but also dispersal of it which occurs by means of penetration into rodent settlements previously free of the disease. During the enzootic period the infection is preserved only at a few points—in the elementary foci. At the time of the next increase in the rodent census and multiplication of parasite vectors the elementary foci serve as places where the first epizootics occur spreading from here to uninfected rodent settlements.

Each of the mechanisms described above is of significance in the natural focalization of plague, and only a combination of them provides for stability of the focus. The latter must be associated chiefly with

the number and stability of elementary plague foci because they provide for the existence of the plague microbe during the most unfavorable, critical period for it.

A brief characterization of the elementary foci as applied to our conditions can be reduced to the following.

Elementary foci ("areas of focalization" in the terminology of B. K. Fenyuk, 1954) in the Aral region constitute individual areas of settlements of the main reservoir of the plague microbe—the great sand rat. Prolonged preservation of the plague pathogen in the elementary foci is explained by the fact that in any years, as observations made have shown, in them continuity of contact with susceptible rodents is most reliably assured by vectors. This requires at least five basic conditions.

The first and most important condition is a minimum census of great sand rats, which is different under different conditions. This explains the fact that the elementary foci are characteristic of large settlements of these rodents. The second condition is at least a relative stability of the great sand rat census, which, as has been shown above, exists only in non-uniform settlements. The third condition can be called "directed movements" of the animals, because on their lines of migration in the non-uniform settlements a fairly constant colonization of the hole-colonies of the great sand rats can be assured reliably by the entrance of more and more new migrants into the vacated holes. Such lines of migration are most distinct in the band and insular settlements. The use of the holes of great sand rats by cohabitant rodents susceptible to the plague increases the chances of reproduction of the pathogen and constitutes the fourth condition for the maintenance of the necessary frequency of contact (multiplicity of hosts in the elementary foci). Finally, the fifth condition is the abundance and stability of the flea census in the great sand rat holes. As we have seen above, the flea census differs considerably in different types of great sand rat settlements.

Each method of assuring contact taken individually usually fails to guarantee the preservation of the pathogen, and only a combination of these methods can provide reliably for the indefinitely long existence of the microbe in a given place. This is why the stable elementary focus is not a very frequent phenomenon.

In the Aral region two main types of elementary foci have been determined: the first is found in the band settlements; the second, in the insular or complex settlements. The first type of elementary focus is represented by large accumulations of great sand rat colonies, usually located at the point of coalescence of several ravines or dry valleys and in their lowlands, particularly on their alluvial fans, where the valleys go out to the sea.

In Fig 6 two examples of such elementary foci are shown on the northwest shore of the Aral sea (Kara-Tyuba peninsula). In the band settlements, with which these elementary foci are associated, the great sand rat census, as has been mentioned above, is relatively stable, re-

covers rapidly after it drops, and does not undergo any deep or prolonged depressions. Dry valleys with band settlements of great sand rats in the clayey desert are not only the most densely populated but also have the richest species composition of rodents. Therefore, in the great sand rat colonies here a rich and varied population of warm-blooded cohabitants and ectoparasites are noted. Their census here is not only higher but also more stable than in other settlements. Finally, as observations of labeled animals have shown, migrations of great sand rats here occur along the ravines and valleys and are directed chiefly from the more populated upper and middle portions of them downward, to the seacoast (Fig 6).

Observations of the settlements of marked colonies have shown that those movements, as has been mentioned above, are made along quite definite and narrow pathways, and there are, so to speak, "favorite" colonies among the animals which are practically never vacant. This is particularly characteristic of the valley lowlands where the migrant flux naturally reaches its greatest density. The marked colonies of great sand rats in the valley lowlands are populated almost twice as vigorously as in the upper or middle courses, where the rodent census is even higher than in the lowlands.

It is clear that specifically in the lowlands and at the point of coalescence of the lateral branches and affluents of the valleys the most favorable conditions exist for permanent (but not necessarily very frequent!) contact between the plague microbe and its natural hosts. Direct confirmation of what has been stated is not only the prolonged presence of the plague pathogen in these places but also abundant findings (compared with other settlements and even with large parts of the same settlement) of entire rodent and other mammalian bones, evidently belonging to animals which died in the holes and great sand rats brought up to the surface of the colonies at the time of cleaning of the holes. In the elementary foci the number of bones in the colonies (the so-called "bone index") exceeds that in sand rat colonies in other places by several times. Several authors have already proved and published material about the bone index as an important feature of elementary foci (Naumov, 1954a; Naumov and Kulik, 1955; Varshavskiy, Rotshil'd and Shilov, 1957). The coincidence of places in which infection is found, in the majority of cases, with areas in which there is an abundance of bones in the great sand rat settlements is well illustrated by Fig 7.

In other parts of the band settlements sometimes a comparatively long (two or three seasons straight) infection of various areas was noted, but it never reached the stability of the elementary foci described above.

Elementary foci in the complex insular settlements, associated with a mosaic landscape of insular and hilly sands in the Aral region along the takyrs of northern Kyzyl-Kumy and the ancient valley of the middle course of the Syr'-Dar' River (Dar'yalyk-Takyr plain) are also found in the same places as accumulations of great sand rat colonies.

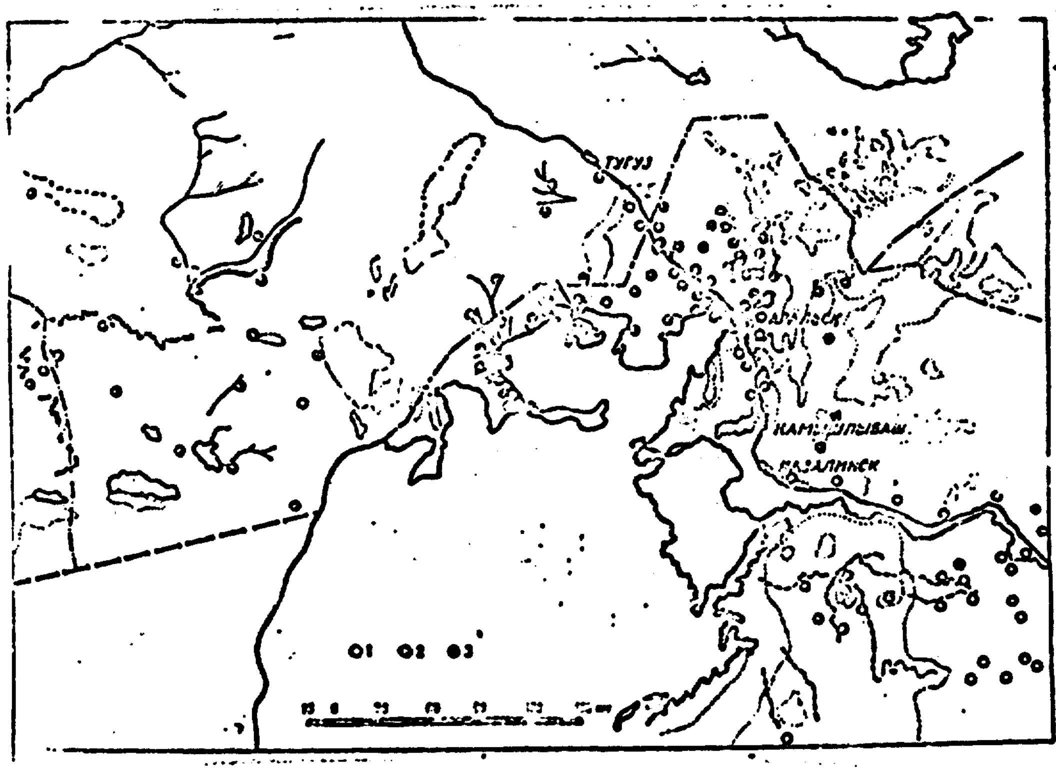

Fig 7

Places in which there is an Abundance of Bones in Great Sand Rat Colonies (after Varshavskiy, Rotshil'd and Shilov, 1957).

1. "epizootic points" with the absence or a small number of bones; 2. places in which there is an abundance of bones, where the epizootic points were not found before 1957; 3. places in which the abundance of bones and epizootics coincide.

These accumulations are located either in patches of black haloxylon among the takyr-like plains, but of necessity in the immediate vicinity of a sand hill or island, or at the boundaries of the sands, frequently on sand ridges going into the takyrs or crossing them.

The characteristics of great sand rat migration here as well as the notably increased intensity of repeated populations of colonies and the substantially greater intensity of interspecies contact by comparison with the continuous settlements of these animals in the sands are quite clearly seen from Fig 8 and Table 4.

Table 4

Repeated Catching of Great Sand Rats in Holes ("Colonies") in Northern Kyzyl-Kumy

Биотоп	Обловлено колоний	Выловлено больших песчанок (в среднем на 1 колонию)						Поймано зверьков других видов (в среднем на 1 колонию)
		при первом облове: VII 1952 г.	при повторных обловах				всего (в % к 1-му облову)	
			VIII 1952 г.	IX 1952 г.	V 1953 г.	VI 1953 г.		
Пески	7	5,1	2,4	2,3	2,9	2,3	192	0,6
Такыры	10	3,4	2,4	1.7	3,4	2,2	235	3,3

1. biotope; 2. colonies caught; 3. great sand rats caught (on the average per colony); 4. at the time of the first catch; 5. at the time of repeated catches; 6. animals of other species caught (on the average per colony); 7. total (in % of the first catch); 8. sands; 9. takyrs.

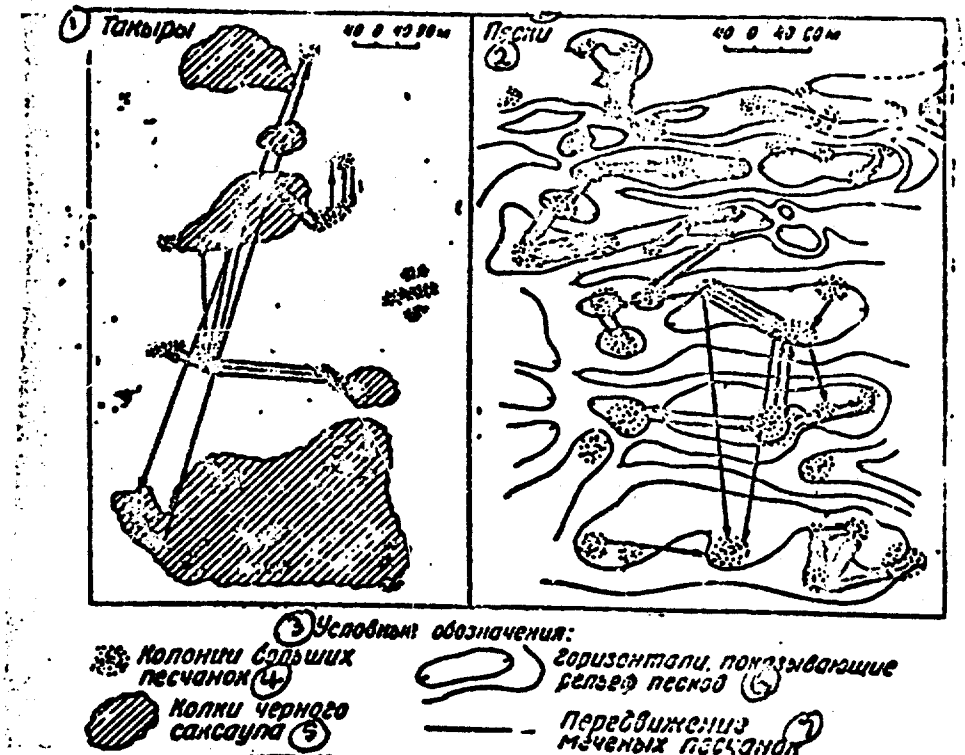

Fig 8

Migrations of Labeled Great Sand Rats in the Sands and on the Takyrs

1. takyrs; 2. sands; 3. key:; 4. great sand rat colonies; 5. clumps of black haloxylon; 6. contour lines showing the relief of the sands; 7. migration of labeled sand rats.

Of particular interest are the accumulations of great sand rat colonies occurring in places along the railroad beds, overland highways, and irrigating system and other landscape changes produced by man.

In such places there is a combination of conditions close to the elementary foci of the band settlements. Therefore, prolonged preservation of the plague microbe is established here. In all these areas the great sand rat census is high and comparatively stable. Its holes are populated by many cohabitants, among which yellow sousliks and red-tailed jirds play the main part. Here, the flea census is high and comparatively stable. Colonies of sand rats caught are populated just as rapidly as in the lowlands of the dry valleys. The great sand rat census returns to its previous condition in such areas in a very short period also, including after extermination operations if they have not been performed on a large scale but are only of a zonal nature (Krylova, Varshavskiy, Besedin, and Shilov, 1955).

Therefore, in these areas also contact of the plague microbe with the hosts is different in its frequency from what occurs in the other parts of the same settlement and particularly in the sandy continuous settlements.

We should like to add that the absence or presence of a small number of rodent bones in such anthropogenic elementary foci (Fig 7) is evidence only of their very recent origin, because of which the bone remnants of animals which died have not yet managed to accumulate here in sufficient numbers. Mention is made about the facts of occurrence of such new elementary foci below.

Apparently, at the boundaries of different types of landscapes in the survival areas of the great sand rats mentioned previously conditions are particularly favorable for the continuous existence of contact between the plague pathogen and vectors and reservoirs of it. Such places can, probably, be particularly stable elementary foci of plague, but they have been inadequately investigated.

Through everything presented above we are attempting to show that in the Aral region the elementary foci may be characterized by definite external characteristics. They occur in band and insular settlements and are absent from continuous settlements in the sands or in the plakor plains. They occur where there are accumulations of great sand rat colonies and are associated with the lines of migration of these animals. On the colonies here more bones brought up from the holes may be found than in other areas of the same settlement. The species composition of these bones indicates the abundance and variety of the cohabitants. Among them frequently the bones of the owners of the hole are far from being most common. In the elementary foci colonies of the great sand rats have a profuse and relatively stable flea population. Finally, these colonies are rapidly populated by newcomers after the hosts have been caught.

Naturally, the quantitative expression of all these signs in various elementary foci may differ considerably. This explains their different stabilities. They appear in large numbers after each exten-

6964

sive epizootic and in the interepizootic period they gradually disappear, whereby a considerable part of them becomes sterile [bacteriologically] quite rapidly. Only a few possess considerable stability. Specifically, these elementary foci become places for the occurrence of new epizootics given a combination of favorable conditions, from where the latter then can spread widely. The biological significance of extensive epizootics consists of the restoration of elementary foci which have died out. It may be supposed that the general stability of the entire focus is directly related to the abundance and degree of stability of the elementary foci existing in it.

At the same time, observations have shown that the elementary foci not only decrease rapidly in numbers after epizootics but can occur in new places as soon as the necessary conditions are created there. In this way new elementary foci appeared specifically in settlements of the great sand rats along the railroad line in the Aral'sk-Kazalinsk section. This section, as was shown by Varshavskiy and Shilov (1956), has only very recently begun to be populated by these rodents, specifically beginning with 1947-1948. However, even in 1952, and then repeatedly at different times for eight seasons plague was found on great sand rats at several points (Khanturtkul', Chumysh, Kamyshlybash, the environs of railroad siding No 92 in the area between Sapak and Kamyshlybash (Fig 7). We have presented the basic results of a study of plague epizootics in the northern and eastern Aral region. They permit us to conclude that for this portion of the Central Asiatic Plain Natural Focus of Plague two ecological forms of existence of the plague microbe in nature, alternating with each other, are characteristic--the epizootic form, when multiplication and extensive dispersal of it occurs, and the enzootic form, when it is preserved in only a few places, in the elementary foci, because there are no conditions for its multiplication as a result of a low census, poor mobility or inadequate susceptibility of its main hosts and vectors. (See the comment by the editorial staff on page 76.) The elementary foci are characteristic of areas with high and stable censuses of great sand rats and an abundance of their cohabitants, that is, they have a distinct multiple-host character. Their stability differs, because the condition of the mechanisms which provide for the necessary constancy of contact between members of the epizootic chain is different. Therefore, in the course of time and for various reasons a considerable part of the elementary foci dies out spontaneously. A process continuing along the same line will lead to the disappearance of the whole natural focus. However, at the time of the next epizootic a restoration of the supply of elementary foci occurs.

Either of the two ecological forms of existence of the plague microbe in nature failed to prevent its preservation and may be the basis for the existence of the natural focus. It is sufficient to mention, in this connection, the steppe souslik [marmot intended?] foci or foci with marmots in the mountains. However, each of them is fraught with the danger of a break in contact and disappearance of the microbe from the local biocoenosis. This break is particularly probable in the

deserts, where a large number of individuals and species of animals participate in the focal processes, and the epizootics are usually of an acute nature. Under such conditions the combination of both forms of existence of the microbe in the natural biocoenoses is probably the basic condition for stability of the focus. Confirmation of this may be seen not only in our data but also in the works of the expedition of I. M. Mamontov (in a manuscript) and in the observations of American investigators in a focus in California; they found the repeated occurrence of epizootics in the same areas, where apparently the pathogen was maintained constantly, and these were nothing other than elementary foci.

It seems to us that everything presented above causes us to draw the following practical conclusions. On epidemiological investigation it is necessary to reckon with the existence of elementary foci. Among the problems of the investigation the finding of elementary foci should be included. The latter requires careful study of the territory and the accumulation of data about the frequency with which the plague microbe is found in different areas. With this aim in view the observance of follow-up in the works of groups is obligatory in the investigation of the same areas. The demonstration of elementary foci is easier made at the beginning or end of epizootics according to cases in which the microbe is found repeatedly in the same places. With respect to its importance the problem of finding elementary foci should be placed second after the primary problem of seeking out acute epizootics, which is to be made chiefly by means of collection and bacteriological investigation of the dead bodies of rodents found on the surface of the ground and mass collection and investigation of ectoparasites from the rodent holes.

The accepted procedure of zoological investigation does not guarantee obtaining the necessary data. Observations of the rodent census and ectoparasite census and making out predictions for changes in it should be accomplished with consideration of the local conditions. For the Aral region, for example, determination of the percentage of colonies populated by the great sand rats and the average number of animals per colony are perfectly adequate. Such observations are expediently made on extensive territories, not just at permanent observation stations ("stationars"). The latter should be confronted with tasks of more thorough study of the most important ecological problems, particularly mobility and contact between animals. An important problem should be the detection, charting and thorough study of colonies of the main species of rodents, which requires prolonged and diverse observation. The methods of such biological recording need to be developed as applied to local conditions.

Finally, supplementation of the existing system of prophylactic measures is needed. Rodent extermination according to the principle of "continuous clearing" of them from the most important territory should be accompanied by late obligatory "clearing" of them in places where plague microbe cultures are isolated from rodents or parasites. In such places combined extermination of rodents and parasites is advisable. Epidemiological detachments and investigation groups themselves should be

able to process the elementary focus found. Such operations can be of the greatest prophylactic significance at the beginning and particularly at the end of the epizootic wave.

Experience has shown the practical possibility of using such a system. There is reason to believe that the combination of extensive operations conducted once or twice with subsequent focal treatment of the elementary foci can accelerate the liquidation of the focus and increase its reliability.

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pp 85-96

Study of the Epizootology and Mechanisms of Focalization of Plague in the Karakalpakskaya Region of Kyzyl-Kumy

Nukus Plague Station

N. Ya. Sharapkova, A. I. Dyatlov, A. P. Tinkina, U. Sorshanov

Introduction

To date there have been practically no published materials on the epizootology of plague in the central portion of the Central Asiatic plain natural focus of plague.

In recent years we made a study of plague epizootics in the western portion of Kyzyl-Kumy in the territory of Karakalpakskaya ASSR and the adjacent portion of the western projection of Bukharskaya Oblast and in the southern portion of Kzyl-Ordinskaya Oblast. The present work is devoted to an analysis of the results obtained.

A plague epizootic was determined in 1924 for the first time in the western portion of Kyzyl-Kumy, in the environs of Ak-Kamysh, to the southeast of Turt-Kul' (Bessonova, 1924; Grekov, 1924; Nikanorov and Knyazovskiy, 1927). Subsequently, beginning with 1948, on the territory which we are describing it has been possible to find plague infection under natural conditions almost every year in one area or another.

The places in which plague-infected rodents and ectoparasites were found to 1956 are shown in Fig 1.

Landscape-Ecological Characterization of the Territory

On the territory of west Kyzyl-Kumy three landscape-ecological zones can be distinguished: northern, central and southern (Kovdyshev, Dyatlov, Rudenchik, 1957). (The term "zones" is not suitable for the various areas of the western portion of Kyzyl-Kumy, because this entire area of desert lies essentially within the same landscape-geographic zone (Editors)). The northern zone includes the region of the dry Zhan-Dar' riverbed and the Bel'tau area. The region of the Bukan-Moreyskiy sand massif, located in the northwest corner of Bukharskaya Oblast can be considered as being partly in this zone.

Characteristic of this zone is the mosaic nature of the landscape with the combination of clayey and sandy desert components. The areas of sand mounds located here are frequently broken up by large takyrs, as a result of which the individual settlements of rodents are separated from one another. At the same time, relatively dense soils assure the prolonged maintenance of great sand rat colonies, even in the case the animals die off in them.

Of the rodents in this area the most numerous are the great sand rats, which find optimum conditions for existence here, as a result of which their highest population density is observed here. The census of

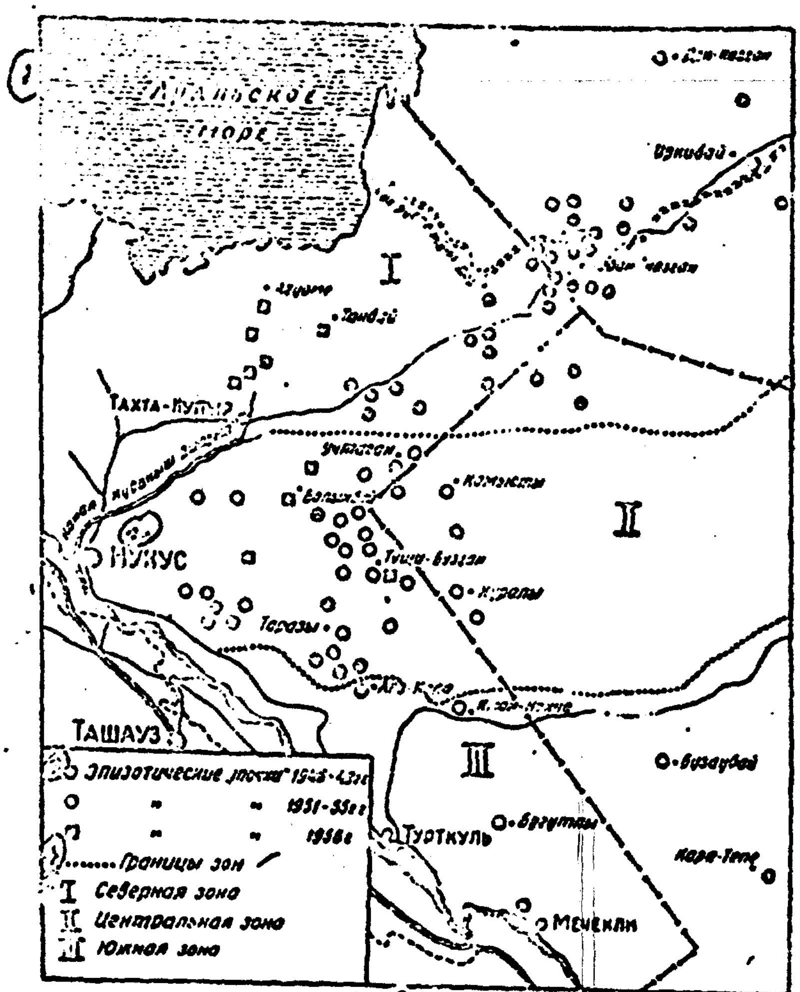

Fig 1.

A diagram of the distribution of "epizootic points" in Karakalpakskaya Region of Kyzyl-Kumy in 1948-1956. 1. Aral Sea; 2. Nukus; 3. epizootic points, 1946-1949; 4. boundaries of zones; I Northern Zone; II Central Zone; III Southern Zone.

meridional jirds /Meriones meridianus/ as well as that of the thin-toed sousliks /Spermophilopsis leptodactylus/ is relatively low; Caspian sousliks /Citellus fulvus/ are encountered from time to time. The five-toed jerboas are predominant here among the jerboas.

The central zone is characterized by sand mounds, which alternate with areas of broken terrain and residual outcrops submerged in the sands. The sands here are not so firmly set as in the northern zone. The vegetation consists basically of psammophytes. The colony density of the great sand rats /Rhombomys opimus Licht./ is less here than in the northern zone. In connection with the scattering of the sands the sand rat colonies are rapidly filled in, and the sand rats have to make them again frequently, which gives rise to a reduction in the number of fleas in the holes. In contrast to the northern zone, the sand areas here are less broken up by takyrs. The main type of rodent in the central zone is also the great sand rat, whereby under favorable conditions the census of these animals can reach high figures, 10-15 per hectare. In connection with the relative continuity of settlements of great sand rats here contact between the animals from different colonies is accomplished more readily. The census of meridional jirds, with the exception of the fringes of sands bounding the river valley of the Amu-Dar' River, is low.

The southern zone is represented by a typical sandy desert, with a large quantity of partly shifting sands. The census of great sand rats in this zone is relatively low. The censuses of meridional and crested jirds, in contrast to what is observed in the northern and central zones, is relatively high here, and these animals are the basic species here. Of the jerboas the three-toed jerboas predominate, and there is almost a complete absence of five-toed jerboas.

Species Composition and Distribution of Fleas

In all, on the territory of Kara-Kalpakskaya ASSR 46 species of fleas and two subspecies belonging to 20 genera and five families have been found (Romanovskiy, Kurepina, Oleynik , Trifonova, 1957). The most numerous species and forms are the following genera: Xenopsylla (seven species), Ceratophyllus (seven forms), Mesopsylla (five species), and Coptopsylla (four species).

The representatives of the genus Xenopsylla are the mass species of great sand rat fleas. In the northern zone (in the area of the dry bed of the Zhan-Dar' River) the main species of fleas is the X. gerbilli, while on the rest of the territory of this zone the main species are X. hirtipes and X. gerbilli. These species of fleas are encountered on the great sand rat and in its holes the year around. Thereby, in the spring months a regular increase in their specific (relative (that is, with respect to fleas of all genera)) census occurs, while in July and August these species become the only flea representatives. Beginning with September their relative census begins to decline, which is associated with the appearance of the autumn-winter species of fleas. Reduction in the relative Xenopsylla census lasts until February, after which their number

again begins to increase.

Thus, in 1954 in May Xenopsylla fleas amounted to 75.0 percent of all the fleas collected; in June, 99.9 percent; in September, 74.0 percent; in November, 39 percent. In 1955 the following respective figures were obtained: in April, 92.0 percent; August, 100 percent; September, 80.0 percent; December, 12 percent. In the autumn-winter season fleas of the genera of Ceratophyllus and Coptopsylla appear en masse. However, during the years of active epizootics and during the autumn period a comparatively high percentage of fleas of the genus Xenopsylla is observed among the ectoparasites.

The constant presence of X. hirtipes fleas on the great sand rat is explained by the fact that they multiply twice a year: in the spring-summer and in the autumn seasons (Kurepina, Kuz'min, Serzhanov, Choreda, 1957).

The number of flea species on the great sand rat and in its holes in the spring is greater than in the autumn, which may be explained by the increased seasonal activity of sand rats, and in connection with this, an increase in the exchange of ectoparasites.

Description of Plague Epizootics

Northern zone. The presence of plague-infected rodents and their fleas was found for the first time in this zone in the spring-summer of 1951 in the area of the dry bed of the Zhan-Dar' River. In all, in 1951 the plague epizootic was recorded in three out of seven investigated "points" and was of an acute nature. In all, 31 plague microbe cultures were isolated including 10 cultures from great sand rats which were found dead; 11 from great sand rats caught alive; one from a dead meridional jird; one from a dead hare; and eight from great sand rat fleas.

There is reason to believe that the plague epizootic here lasted until 1951. The pronounced dissociation of the plague colonies in cultures, the delay of glycerin fermentation in a large number of the strains isolated and reduced virulence in them can constitute confirmation of this.

In 1952, the presence of a plague epizootic in the Zhan-Dar'region was determined in six places, whereby 24 cultures were isolated (20 from great sand rats; one, from a meridional jird; one, from a hare; and two, from fleas). In the spring, the epizootic was of an acute nature, while in the autumn only two cultures were isolated (one from a great sand rat and one from a meridional jird). Of six epizootic "points", only one was a "point" in the 1951 epizootic.

In 1953, 13 epizootic "points" were recorded, and 34 plague microbe cultures were isolated (28 cultures from great sand rats and six, from their fleas). The epizootic occurred in an acute form during the spring, summer and autumn seasons.

In 1954, on this territory, cultures of the plague pathogen could be isolated only during the period of the spring-summer investigation. In all, at seven epizootic "points" 33 cultures were isolated (15 from

great sand rats; 17, from fleas taken from great sand rat holes; and one, from fleas combed off great sand rats). The epizootic was of an acute nature and the infection rate of rodents for various "points" varied from 0.3 to 3.9 percent. Beginning with the autumn of 1954 it was impossible to find plague in the Zhan-Dar' region. The cessation of the epizootic may have been due to work on the extermination of great sand rats. Beginning with 1951, that is, beginning with the time of detection of the epizootic, through 1956 inclusive, great sand rats were exterminated every year in the places in which epizootics were detected. In all, during this period an area totalling 310,600 hectares was treated.

In the region of the dry bed of the Zhan-Dar' River a plague epizootic in rodents lasted for four years--from 1951 through 1954. In this time 25 epizootic "points" were demonstrated here, and 122 cultures of the plague microbe were isolated; of these, 84 cultures were obtained from great sand rats; two, from meridional jirds; two, from hares; and 34, from fleas taken from the holes and the fur of the great sand rats.

In our opinion, the separation of the sandy areas contributes to the prolonged maintenance of plague infection in this region. Epizootics appeared and were recorded here simultaneously on relatively small areas and did not take on a diffuse character. Rodents sick with plague and infected fleas were most often detected on the sweep of sand massifs, at junction places of sand hills and takyrs. It should be noted that in the majority of the epizootic points the existence of the plague infection could be determined only for one season. Twice at various time intervals the epizootic was observed only in individual "points" (Chaban-Kazgan, Baychuvak, Nagay-Shagay).

On the remaining territory of the northern zone the epizootic was recorded from 1951 through 1956 inclusive. In 1951 one culture of plague microbe was obtained in the region of the Bukan-Mereyskiy massif from fleas combed off great sand rats. In the spring of 1952 at this point great sand rats were exterminated over an area of 5,110 hectares.

In the spring of 1954 the epizootic in this region was repeated, but the cultures were isolated from territory located directly on the boundary of the area treated.

In the spring of 1955 the epizootic was recorded for the first time in the western portion of the Bel'tau area, in the region of Agurme well. At the time of the autumn investigation of this region no epizootic could be found.

In the spring of 1956 here an epizootic was demonstrated at four "points", in which 47 cultures of the plague pathogen were isolated. Thereby, 23 cultures were obtained from great sand rats, 23 from fleas, and one from ticks collected from the holes of great sand rats; the species categories of the ticks remained undetermined. Aside from the 47 cultures named, two cultures were isolated from great sand rats caught in the central part of the Bel'tau area (Tanbay well).

In the autumn of 1954 and the spring of 1955 the epizootic occurred in the region of the Don-Kazgan well (95 kilometers to the north of the Chaban-Kazgan well). From 1952 through 1954 the epizootic

occurred in other areas of the northern zone (Saksaul'naya Dacha, Buzgul, Buzganak and others). In all here 11 epizootic "points" were detected in this period, and 80 cultures of the plague microbe were isolated; of these 50 cultures were isolated from great sand rats; six, from meridional jirds; two, from Lichtenstein jerboas [Eremodipus lichtensteini]; two, from ticks; 80, from great sand rat fleas; one, from fleas combed off the mottled polecat (Vormela peregusna). At eight "points" the epizootic was repeated in the years which followed (Chabon-Kazgan, Buken, Buzgul, Buzganak, Magay-Shagay, Don-Kazgan, Agunmo, Uzun).

In the autumn of 1956 in the entire northern zone, despite careful investigation, no plague microbe cultures were isolated.

Central zone. For the first time in this area a plague epizootic was found in December 1948, although there is reason to believe that it occurred here in 1947. In 1948 the epizootic was acute and included a considerable area—more than a million hectares. From December 1948 through July 1949, 21 epizootic "points" were detected and 97 plague microbe cultures were isolated (80 from great sand rats; two from meridional jirds; three from thin-toed sousliks; two from weasels; ten from fleas).

Beginning with the autumn of 1949, despite careful investigation of this territory, no plague infection could be found in nature until 1954.

In the spring of 1954 the presence of plague was established at one "point" (Uchtagan mound), whereby one culture was isolated from a great sand rat.

In 1955 an acute epizootic occurred in the southern part of this area to the north of the Sultan-Uizdaga range. In all, eight epizootic "points" were found here, and 118 plague microbe cultures were isolated; of these, 38 cultures were from great sand rats; one, from the meridional jird; 13, from fleas taken from the fur of the jirds; 65, from fleas caught in the holes of the jirds; and one, from a nymph of the Hyalomma tick combed off the fur of a great sand rat.

It should be noted that the large number of cultures obtained from fleas in 1955 is explained by the examination method. In a fixed area, located 20 kilometers to the south of Taraza well, in a number of cases all the fleas collected at the entrances to the holes were investigated individually. As a result of individual examination 58 cultures were isolated, and by means of group cultures only 20 cultures were isolated. We shall dwell in detail on this problem below in the analysis of factors in the natural focalization of plague in Kyzyl-Kumy.

Of the total number of 78 cultures isolated from fleas 73 were obtained from fleas the species classifications of which were accurately determined. It was found that the largest number of cultures were given by fleas of the genus Xenopsylla; 52 cultures were isolated from X. hirtipes; 20 cultures from X. gerbilli; and only one culture, from Ceratophyllus tersus.

In the autumn of 1954 an acute epizootic was detected to the north of Ayaz-Kala fortress, where three epizootic "points" were estab-

lished and 11 cultures were isolated (nine from great sand rats and two from fleas).

In 1956 on the territory of the zone being described a plague epizootic occurred at four "points"; 13 cultures were isolated; of these three were from great sand rats; ten, from fleas. An acute course of the epizootic was noted in only one "point" (Tushchi-Buzgan), from which nine cultures of the plague pathogen were isolated (one from the great sand rat and eight from fleas collected at the entrances to the holes). In the remaining "points" (Vysota 131, the Balykbay natural boundary, and Koc-Kuduk) isolated cultures were obtained.

The Balykbay natural boundary was one of the areas on which the Nukus plague station made zoological and parasitological investigations at a fixed point there. The material for the investigation was taken from this fixed point every month during 1955 and 1956; however, it was possible to isolate only one culture from fleas combed off a great sand rat in May 1956.

In the autumn of 1956 no epizootic was detected on the territory of the zone being described. It should be noted that in the southern part of this zone in 1955 and 1956 extermination of great sand rats was conducted over a total area of 367,000 hectares.

In all, in the central zone during the entire period of investigation of it—from 1948 through 1956—35 epizootic "points" were recorded and 240 plague microbe cultures were isolated, including cultures from great sand rats, 131; from meridional jirds, 3; from thin-toed sousliks, 3; from weasels, 2; from fleas, 100; and from Hyalomma ticks (nymphs) combed off great sand rats, 1. The epizootic was repeated at eight "points" (Kuraly, Ul'ken-Kara-Sor, Sadyk-Tyube, Bayniki, Vysota 131, Tushchi-Buzgan, Uchtagan and 20 kilometers to the south of Taraza well).

Southern zone. After the epizootic in 1924 in the environs of Ak-Kanysh of Turtukul'skiy Rayon a new epizootic was recorded here only in the spring of 1949 at one "point" (Kazan-Kochka), where nine cultures of the plague microbe were isolated (four from great sand rats; three, from yellow sousliks; and two, from fleas).

From 1949 through 1952 the epizootic was not demonstrated anywhere in the southern zone. In the spring of 1953 with the aid of a biological test a single plague culture was isolated from meridional jirds caught in the region of Mechekla village. In the spring of 1954 on new areas of this zone three epizootic "points" were found, from the territory of which nine cultures of the plague microbe were isolated (five from great sand rats and four from fleas).

In 1955 only two epizootic "points" were detected, and six cultures were isolated (four from great sand rats and two from fleas).

In all, from 1949 through 1955 on the territory of the southern zone seven epizootic "points" were recorded and 25 cultures of the plague pathogen were isolated, of which 13 were obtained from great sand rats, three from yellow sousliks, eight from fleas, and one from the meridional jird.

Therefore, from 1949 through 1956 inclusive in western Kyzyl-Kum

plague epizootics among great sand rats were repeated every year (aside from 1950), but they occurred on various areas at different times and with different intensity. Thus, for example, in the northern zone the epizootic was recorded every year from 1951 through 1956, and in the majority of cases was of an acute character (44 epizootic "points" were recorded and 268 cultures isolated), whereas in the southern zone the epizootic was noted only in various years (1949, 1953, 1954 and 1955), whereby it took on a local character. In all, during this period of time only seven epizootic "points" were found and 25 cultures isolated.

During the entire period being described over the entire territory of western Kyzyl-Kumy, 86 epizootic "points" were recorded, and 533 plague microbe cultures were isolated; thereby, 327 cultures were isolated from great sand rats; one, from meridional jirds; three, from thin-toed sousliks; three, from Caspian sousliks; two, from weasels; two, from hares; two, from ticks combed off the great sand rats and meridional jirds; one, from ticks caught in holes; 180, from fleas taken from the fur and holes of the great sand rats, and one from fleas combed off the mottled polecat. The epizootic was repeated at 16 "points" in the years which followed.

The majority of the fleas was investigated without determining their species classification, but in those cases where the fleas were determined to the species level the plague microbes were isolated mainly from Xenopsylla hirtipes (59 cultures), X. gerbilli (28 cultures). In addition to this, three cultures were obtained from Ceratophyllus tersus. Among the other species of fleas none were found to be infected with plague.

The Mechanism of Natural Focalization in Western Kyzyl-Kumy

Proceeding with the analysis of mechanisms of natural focalization of plague in western Kyzyl-Kumy we should first of all dwell on the data obtained in the established area mentioned above, which was located on the territory of the central zone, 20 kilometers to the south of Taraza well. The area was divided into squares measuring about 100 hectares on the average. The diagram of the arrangement of the squares is shown in Fig. 2.

The first six cultures were isolated on this area in May 1955; of these, three cultures were obtained from great sand rats; one, from a meridional jird; and two, from fleas collected at the entrances to the holes.

From June to December 1955 on this fixed area every month various cells were investigated, on which all the existing colonies and the degree to which they were inhabited were taken into consideration, all the animals living in the colonies were caught, and the maximum number of ectoparasites were collected in the entrances to the holes of the colonies. [the term "fixed area" denotes area serviced by a plague station].

Square No. 1 with an area of 100 hectares was investigated in July. In all, 116 colonies were demonstrated; of those 79.2 percent were inhabited (Fig 3).

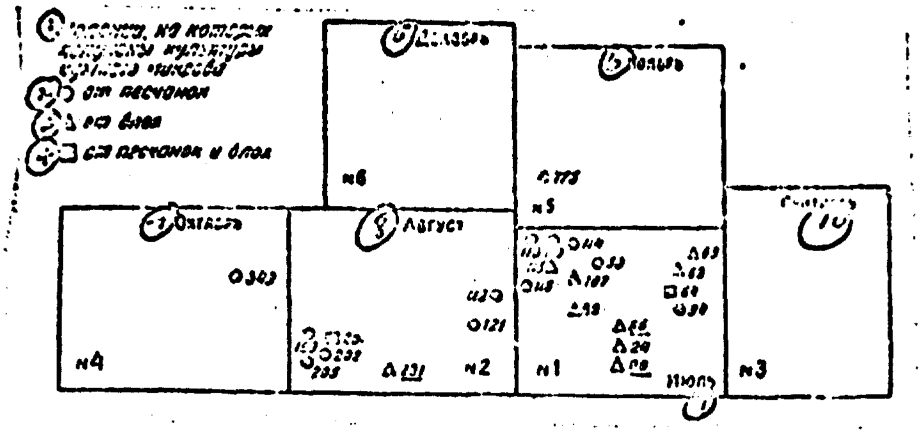

Fig 2

Diagram of Distribution of Squares (with an Area of about 100 Hectares each) in the Fixed Area in the Vicinity of Taraza Well (Central Zone). Colonies No 231 (square No 2), 66 and 80 (square No 1) were uninhabited. 1. colonies in which plague microbe cultures were obtained; 2. from sand rats; 3. from fleas; 4. from sand rats and fleas; 5. December; 6. November; 7. October; 8. August; 9. July; 10. September.

The population density of the great sand rats in this square was low, amounting to 1.9 animals per hectare; the density of the meridional jirds reached 8-10 animals per hectare. In this square three places were detected where infected rodents were found among the rodents and fleas living in these places.

In the northeastern part of the square plague-infected great sand rats and their fleas were found in four colonies. Colony No. 64 can be considered the center of this epizootic spot. On examination of this colony on 13 July, four great sand rats were caught, two of which were found to be infected with plague and with bacteriemia. Of three Xenopsylla gerbilli fleas combed from the fur of these sand rats a plague culture was also obtained. From the entrances to the holes of colony No. 64, 63 fleas were collected and subjected to individual examination (39 X. hirtipes and 24 X. gerbilli), from which 35 cultures of the plague microbe were isolated (24 from X. hirtipes and 11 from X. gerbilli). At the time of a second examination of this colony eight days later (21 July) 75 fleas were collected and examined individually; from these one specimen of X. gerbilli gave a plague microbe culture.

In the vicinity of colony No 64, three other infected colonies were found—Nos 68, 69 and 94. From colony No 68 a plague microbe culture was isolated from X. hirtipes fleas which had been combed from a single great mole rat; fleas from the holes were not investigated. From the entrances to the holes of colony No 69 35 fleas were collected;

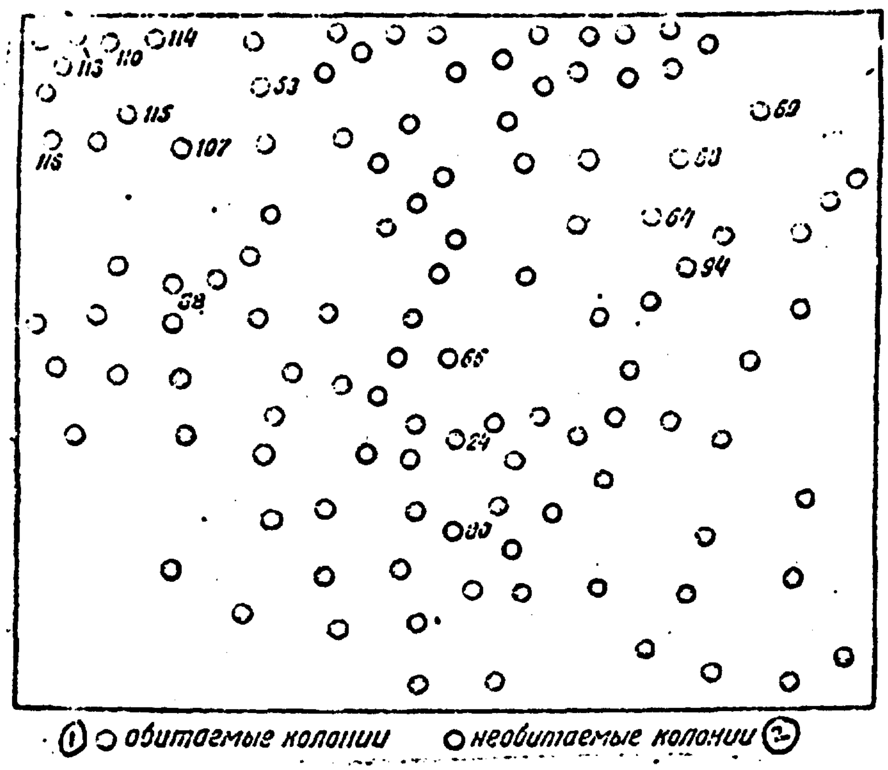

Fig 3

Diagram of Distribution of Great Sand Rat Colonies (from the Example of Square No 1). The numbers are placed next to the colonies from which cultures of the plague microbe were obtained (compare with Fig 2). The black circles are inhabitable colonies; the clear circles, uninhabitable. 1. inhabitable colonies; 2. uninhabitable colonies.

this included 32 X. hirtipes and three X. gerbilli; from the latter one culture was isolated. From colony No 94, four great sand rats were caught; on culture of the organs of one of them a growth of plague colonies was obtained. On investigation of fleas collected at the entrances to the holes the results were negative.

In the central part of the square in three adjacent colonies, Nos 66, 24 and 80, the presence of plague infection was found only in the fleas. From colonies No 24 and No 66 the plague microbe culture was obtained from X. hirtipes fleas combed from the great mole rats. Investigation of the mole rats themselves and of the fleas from the holes gave a negative result. In colony No 80 there were no rodents; at the entrances to the colony, 19 X. hirtipes fleas were collected; group culture of these gave only one plague microbe culture.

In the northwest corner of the square, five colonies were demonstrated with plague-infected rodents and three colonies with infected fleas. Colonies No 115 and 107 may be taken as the center of this epizootic spot.

The investigation of two great sand rats caught from colony No 115 on 15 July gave a negative result. However, on individual investigation of 126 fleas (65 X. hirtipes and 61 X. gerbilli) collected at the entrances to this colony on 21 July, 16 plague microbe cultures were isolated (11 from X. hirtipes and 5 from X. gerbilli). A second examination of the fleas collected from the holes of this colony in August, November and December gave a negative result. The finding of a mummified great sand rat cadaver during the process of digging up colony No 115 on 25 December is interesting. At the same time, 227 fleas were collected among which there were 157 Paradoxopsylla teretifrons, 11 Xenopsylla hirtipes, 24 X. gerbilli, 20 Ceratophyllus tersus and 15 fleas of other species. Investigation of these fleas gave a negative result.

From colony No 107, two great sand rats were caught on 15 July in which no plague was found. However, one X. hirtipes flea was combed from these great sand rats which on culture gave a growth of plague colonies. At the entrances to the holes of colony No 107, 41 fleas were collected (31 X. hirtipes and 10 X. gerbilli) on individual examination of which six plague microbe cultures were isolated (five from X. hirtipes and one from X. gerbilli). Investigation of the fleas collected a second time on 18 August gave a negative result.

To the northwest of colony No 107 and 115 were colonies Nos 114, 110, 113, and 116. From these colonies ten great sand rats were caught among which five were found to be infected with plague (in colonies Nos 110, 113 and 116, one sand rat each, and in colony No 114, two sand rats). On examination of the fleas combed from the sand rats none was found infected with plague.

Aside from this, one plague microbe culture was isolated from a great sand rat caught in colony No 53 which was located to the northeast of colony Nos 107 and 115. Among the fleas from colony No 53 none was found to have plague. Finally, another culture was obtained from this epizootic spot in 20 fleas combed from two great sand rats taken from colony No 88.

The fact attracts attention that the great sand rat colonies which had died out in this square were located in the northern area between the northwest and northeast epizootic spots. The living colonies were located to the southwest and southeast, where none was found infected (see Fig 3).

Square No 2, 120 hectares in area, was investigated from 17 through 23 August. One hundred five colonies were investigated; of these, 65.2 percent were inhabited. The density of great sand rats amounted to 1.3 animals per hectare. In this square two epizootic spots were isolated: in the southwest and east of the square.

In the southwest of the square plague-infected rodents and fleas were found in three colonies. From colony No 201, six great sand rats

were caught; from one of these a plague microbe culture was isolated. One culture, in addition, was isolated from 36 X. hirtipes fleas collected from the entrances to this colony. In colonies Nos 198 and 202, located to the southwest of colony No 201, six great sand rats were also caught, and of these one was infected with plague. Investigation of the fleas gave a negative result. From colony No 205, five great sand rats were caught one of which gave a culture of the plague microbe. Among the fleas from this colony none had plague.

In the eastern part of this square, two colonies were detected (Nos 121 and 119) with infected rodents. No plague microbes were obtained from the fleas.

Almost all of the extinct colonies in this square were concentrated in the southwest corner, that is close to the area in which the infected colonies were located.

Square No 3, 99 hectares in area, was investigated from 20 through 30 September. On this square there were 99 colonies, and of these 57.3 percent were inhabited. No plague-infected great sand rats or fleas were found in this period. In this square there was also a focal arrangement of uninhabited colonies, chiefly in the center.

Square No 4, 120 hectares in area, was investigated from 20 through 30 October. One hundred and thirty-three great sand rat colonies were counted; of these, 54 percent were inhabited. In this square a single epizootic "point" was found—colony No 349. Among three great sand rats caught in it, one was found infected with plague. The infected sand rat did not have any visible pathological changes in the internal organs: on culture of the spleen and liver isolated colonies grew out. No plague-infected ectoparasites were found.

Square No 5, 99 hectares in area, was investigated from 20 through 30 November. On it 131 colonies were found including 48.1 percent which were inhabited. A single plague microbe culture was isolated by means of infecting a test rodent with the organs of four great sand rats caught in colony No 476. In the organs of sand rats included in the test there were no visible pathological changes; cultures of the organs in agar containing phage antiserum gave no growth of the plague colony; the test rodent died on the 11th day. Investigation of the ectoparasites gave a negative result.

Square No 6, 100 hectares in area, was investigated in December. On it there were 98 colonies; of these, 20 percent were inhabited. The plague-infected rodents and ectoparasites were not found.

On the basis of data obtained through the investigation of a fixed area, a marked reduction could be noted in the number of inhabited colonies in the autumn-winter season. Simultaneously with this a gradual reduction in the infective nature of the area was observed also, specifically in the percentage of infected colonies (in July there were 12 percent of them; in August, 5.6 percent; September, 0 percent; October, 0.7 percent; November, 1.1 percent; December, 0 percent) and in the percentage of infected rodents (in July, 4.5 percent; August, 2.3 percent; September, 0 percent; October, 0.7 percent; November, 0.7 percent; December, 0 per-

cent). Among the infected great sand rats there was a marked reduction in the incidence of cases of acute plague, with the presence of bacteriemia. Thus, in July bacteriemia was noted in six out of nine infected great sand rats; in August, two out of five great sand rats had bacteriemia; in the autumn months there was no bacteriemia in the infected great sand rats. Simultaneously with this a reduction in the number of infected fleas was observed. For example, in July on group examination of 3,657 fleas, seven plague cultures were isolated; from individually examined fleas, numbering 867, 58 cultures were isolated (40 from X. hirtipes and 18 from X. gerbilli); in August on examination of 2,269 fleas by group cultures only two cultures were isolated (from X. hirtipes); on individual examination of 572 fleas none was found infected with plague; finally, from September through December (end of the investigation) not a single infected flea was found in the examination of 740 fleas.

Reduction in the intensity of the epizootic in the autumn-winter should be explained, we believe, by the reduction in the activity of great sand rats and reduction in their colony density, as well as by the reduction of the number of fleas of the genus Xenopsylla, which are the main vectors of plague on the territory being described. In the autumn-winter season species of fleas appear which play a very small part in plague epizootology.

The infected colonies were arranged on the fixed area in individual groups (1-8 colonies each) at a distance of 200-500 meters from one another between non-infected colonies.

All these data make it possible to express the idea that the epizootic has a "focal" course in great sand rat colonies, which might be explained chiefly by the mode of life of these sand rats, which are encountered in groups of several animals per colony, as well as by the abundance of fleas in the latter.

In cases where the infection has an acute course in the great sand rats, infected fleas may attach themselves to sand rats from neighboring colonies seeking temporary shelter here. Therefore, new plague foci may be created. Possibly also the plague-infected fleas are scattered by the sick sand rats. The spread of plague to neighboring colonies as the result of intraspecies contact between the great sand rats can apparently occur over a comparatively short distance. Through our observations a low degree of intensity of intraspecies great sand rat contact in the holes was noted; these animals usually visited only the nearby colonies. The existence of relatively great distances between the various foci (epizootic spots), of the order of 200-1000 meters from one another, can be explained by the carriage of infected fleas over these distances by other animals which frequently visit the colonies of the great sand rats, particularly, the meridional jird, thin-toed souslik, and mottled polecat.

The "focal" infection of great sand rats and their ectoparasites can also be confirmed by the following observation data. In May 1956, in investigating the environs of Bushchi-Buzgan well, one plague microbe culture was isolated from a great sand rat which had been caught two

kilometers to the northeast of the well and three cultures from fleas collected in the same place. After five-eight days a second collection of fleas was made from the holes around the well and along routes 1.5-3 kilometers in length located to the north, south, west and east of the well. On each route from 248 to 395 fleas were collected; from each batch of fleas 8-12 cultures were made. All the cultures of the fleas collected around the well on the routes to the north, east, and south of it gave negative results. Only from the eight flea cultures (X. hirtipes) collected three kilometers to the west of the well did five cultures grow out. The same situation was noted on investigating the western part of Bol'tau.

Without dwelling on the characterization of the pathological changes in plague-infected great sand rats it should be noted that both in the [illegible] area and on the entire territory being described the majority of cultures were isolated from great sand rats without visible pathological changes.

The bodies of great sand rats which died of plague were found only on investigation of the northern zone, where of 173 cultures isolated from great sand rats, 14 were obtained from animals found dead. In the central and southern areas all the cultures were isolated from great sand rats caught alive.

All the cultures which we checked were glycerin-positive, although in various cases a delay in glycerin fermentation in liquid medium was noted up to 16 days.

We studied virulence chiefly in cultures isolated in 1955 at the Tarema station. All the strains which we isolated were virulent; however, in some cases various guinea pigs infected with doses of 100 and 100,000 microbe bodies survived. We could not find any considerable difference in the virulence of strains isolated in different months—from July to November.

Conclusions

1. The main reservoirs of the plague microbe in the western part of Kyzyl-Kumy are great sand rats. Other species of rodents—meridional jirds, hares, the thin-toed souslik, etc.—are involved in the epizootic only during periods of the acute course of the latter among the great sand rats.

2. Of the fleas encountered on this territory, fleas of the genus Xenopsylla, chiefly X. hirtipes and X. gerbilli, are of principal epizootological significance. During the entire period of work only three cultures were isolated from other species of fleas (from Ceratophyllus tersus fleas).

3. In the three landscape-ecological zones established for western Kyzyl-Kumy, the epizootics proceed differently.

For the northern zone (the region of the dry Zhan-Dar' riverbed and the territory adjacent to it with its mosaic relief) a relatively long course of epizootics is characteristic; however, they do not acquire

the nature of being diffuse. At the same time, at the same "points" plague is usually maintained a relatively short period of time. For the central area more diffuse but rapidly terminated plague epizootics are characteristic. In the southern area only local epizootics are noted.

4. Plague epizootics among great sand rats are of a "focal" nature. This may be explained chiefly by the relatively little contact between sand rats from distant colonies and the abundance of fleas in the latter.

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Some Results and Prospects of Study of the Natural Focalization of Plague on the Territory of the Chinese People's Republic

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The Chinese People's Republic occupies an extensive territory with tremendous reserves of natural resources which constitute the material basis for the socialistic reconstruction of the Republic. It is sufficient to say that the Chinese People's Republic is in fourth place in the world with respect to coal reserves, coming after the USSR, United States and Canada. According to some calculations, the water power resources of China amount to 150,000,000 kilowatts, which, as is well known, are mainly concentrated in the Southwest of the country. At the same time, China has at its disposal considerable reserves of iron ore, which before the revolution was estimated at 10,000,000,000 tons.

At the same time, the territory of the Chinese People's Republic is very diverse with respect to its geographic characteristics, fauna and flora. The latter has created the basis for the existence of natural foci of the various diseases of man with different etiologies-- protozoan, bacterial, and virus. These diseases do tremendous harm to the health of the population, which may become a major check to the development of socialism in China. This applies particularly to diseases of protozoan and virus etiologies as well as to helminthic infestations. Among the diseases with a natural focalization is plague.

Before the victory of the people's revolution plague was one of the widespread diseases in China with an exceptionally high mortality rate. The history of plague in China has been extensively discussed in the literature, and therefore there is no reason to dwell on this subject here.

After the revolution, under the direction of the CP and the government of the People's Republic, through the disinterested assistance of the Soviet Union the morbidity rate among the people was markedly reduced. At the present time, it is limited to isolated cases of the disease, whereby because of modern methods of treatment of plague the absolute majority of the patients recovers.

Reduction of the endemic nature of plague was achieved by extensively developed measures for rodent extermination, the reservoirs of the plague microbe. It is sufficient to say that on the territory of Northeast China-- in the Kirin Province (which in the past was one of the most affected by plague) extermination operations were conducted over an area of 5,000,000 hectares in 1956, which constituted almost 90 percent of the territory potentially dangerous because of plague. At the present time, all the results of extermination operations against rodents have not been summarized for the entire territory of China; nevertheless, it should be stated that these operations have become one of the chief divisions of

plague prophylaxis.

It should be noted that the control of rodents in China is not only the work of plague institutions; large masses of workers, organized by popular committees on various levels under the supervision of specialists in the plague institutions participate in it. This measure in the People's Republic of China is one of the divisions of general control of sanitary culture, known as the patriotic sanitation movement.

Along with rodent extermination, people are being vaccinated against plague with living vaccine according to the epidemic indications. This vaccine is prepared, as was recommended to us by the Soviet expedition (B. N. Pastukhov, M. P. Pokrovskaya and others), from the EV strain.

The practical elimination of plague in people in China is not at all a circumstance which permits us to slacken our attention to matters of plague prophylaxis. Conversely, we are attempting to raise problems of plague prophylaxis to an even higher level, directed at the elimination of the natural focalization of plague proper. This principle obliges us to carry out scientific research work on the study of the epidemiology and epizootology of plague in its natural foci in addition to practical measures for the control of plague.

Unfortunately, the shortage of highly qualified cadres of specialists in this field in the Chinese People's Republic does not permit developing these operations on the scale required at the present moment by the interests of public health of the Republic.

Before 1947, the study of rodents as possible sources of plague was conducted inadequately. Foreign authors (Allen, Sowerby and others) mainly concentrated on problems of classification of rodents, and only some studied the epizootological role of rodents (D. K. Zabolotnyy, Wu Lien-tieh, Jurauchi, Casca, and Kato). Special attention was given to the latter problem by D. K. Zabolotnyy and Wu Lien-tieh who determined the existence of plague among tarbagans in Manchuria and Inner Mongolia. Japanese investigators, who carried out their work in Northeast China and in Inner Mongolia, determined the existence of plague among brown rats /Rattus norvegicus/. As far as the role of Daurian souslik /Citellus dauricus/ is concerned, although they attracted the attention of these investigators, they did not give the solution of the problem of plague in souslik.

After the revolution and with the aid of Soviet specialists (I. I. Rogozin, I. N. Mayskiy and others) the study of the epizootological role of rodents and their fleas began to be conducted on a large scale, particularly in Northeast China and Inner Mongolia. At the same time, problems of rodent classification continued to be studied on a broad scale.

At the present time, the existence of more than 140 species of rodents has been determined on the territory of the Chinese People's Republic. The following species of rodents are of epizootological significance in plague: 1) the Daurian souslik-- Citellus dauricus (Northeast China and Inner Mongolia); 2) the long-tailed souslik-- Citellus undulatus (Sinkiang); 3) the tarbagan-- Marmota sibirica (Inner Mongolia); 4)

the Altay marmot-- Marmota baibacina (Sinkiang, Tsinghai); 5) the long-tailed marmot-- Marmota caudata (Sinkiang); 6) the Mongolian jird-- Meriones unguiculatus (Inner Mongolia); 7) the Daurian pika-- Ochotona daurica (Inner Mongolia). [Daurian=Manchurian]

Aside from the species listed, in some areas of Sinkiang-Uigurian Autonomous Oblast (T'ingho, Mangas, Wucha and others) recently the existence of colonies of the crested jird (Meriones tamariscinus) and of the great sand rat (Rhombomys opimus) has been found. Study of their epizootological significance constitutes the task of forthcoming research work in those areas.

All these species of rodents listed are characteristic of the northern foci of plague. Materials on the study of the northern foci of plague show that rodents of the subfamily Murinae are involved in plague epizootics-- the brown rat (Rattus norvegicus), the house mouse (Mus musculus) and others, as well as members of the subfamily Cricetinae-- the rat hamster and the Daurian hamster (Cricetulus triton and Cricetulus barabensis).

In speaking about rodents in the southern foci-- in the provinces of Fukien, Kwangtung, Yunnan-- it should be noted that they have been inadequately studied. In connection with this, there is a sparsity of data on the epizootological significance of wild rodents. Nevertheless, the fact that a culture of plague microbe has been isolated from Callosciurus erythraeus [squirrel] speaks for the possibility of plague epizootics among them, which should be confirmed by the forthcoming research work in those foci.

In the southern foci, as is well known, synanthropic rodents are of principal epidemiological importance. The main species of them is the black rat (Rattus rattus) and its subspecies, R. r. flavipectus. The materials which we have at our disposal at the present time are evidence of frequent epizootics among rodents of this species.

Before the revolution the only known vector of the plague was the flea Xenopsylla cheopis, which had rats as its main host and was encountered throughout China. Research work done after the revolution revealed the epizootological significance of other species of fleas also, namely:

Species of flea	Main host	Location
1. Ceratophyllus tesquorum sungarus	souslik	Inner Mongolia, Northeast China
2. Frontopsylla luculenta	souslik	Inner Mongolia
3. Oropsylla silantiewi	tarbagan	Sinkiang, Tsinghai
4. Callopsylla dolabris	tarbagan	Sinkiang
5. Neopsylla bidentiformis	a number of species	Inner Mongolia
6. Xenopsylla cheopis	rats	all foci of China
7. Leptopsylla segnis	number of species	Fukien, Kwangtung, Yunnan

In accordance with the comments made by Soviet specialists (B. N. Pastukhov, M. P. Pokrovskaya) our attention was drawn to investigating ticks. It was found that the main species of ticks parasitic on the tarbagans is Ixodes crenulatus; on the souslike, Haemaphysalis. In 1955, in Betse district, cultures of the plague microbe were isolated from certain ixodial ticks, the species of which was not determined because of the absence of specialists.

In a number of matters of the study of the natural focalization of plague the problem of the preservation of the plague microbe in the interepizootic (winter) period is of great practical importance.

As the observations of Soviet authors have shown (D. K. Zabolotnyy, A. A. Chumilina, N. A. Gayskiy, I. S. Tiner, P. N. Strpnitskiy and others), hibernating rodents and their ectoparasites can spend the winter with the infectious principle. It must be supposed that these rules and regulations also apply in the northern foci of China.

Japanese investigators (Kato, Hati and others) who worked in the past in northeast China believed that plague is preserved in the inter-epizootic winter period by brown rats. At the present time, we have no data at our disposal on this subject.

On the territory of the former province of Jeho in 1954 the first plague bacillus culture from a souslik was isolated on 15 April. In one of the regions of the canton of Betse in Northeast China in 1953 the first plague bacillus culture was isolated from a group of fleas Ceratophyllus tesquorum sungarus even earlier, on 7 April. The fleas were collected from a single souslik hole. It should be noted that in the same area active fleas were found in dug up rodent holes from November through February. They all belonged to the species C. t. sungarus.

All these facts together make us consider the possibility that sousliks infected with plague and their ectoparasites spend the winter together.

Discussing certain details from the study of the epizootic process in plague among rodents in the natural foci of this infectious disease, it should be stated that in Northeast China and Inner Mongolia a mass migration of brown rats is observed in the summer to the open spaces. In these spaces the rat holes in various cases are connected with the holes of Daurian sousliks. It is perfectly natural that under such conditions an exchange of ectoparasites between these species of rodents is entirely possible. To this it should be added that a close connection between rats and sousliks is established specifically in the vicinity of inhabited places. Epizootological and epidemiological significance of close contact with rats is illustrated, for example, by the fact that in 1955 the body of a brown rat was found 1.5 kilometers from a village, and a culture of the plague microbe was obtained from it. These materials show that domestic rodents are involved in the plague epizootic among field rodents, and people are infected from the former through the ectoparasites. A number of Soviet investigators have indicated the possibility of such a mechanism also (I. I. Rogozin, B. N. Pastukhov, B. K. Fenyuk and others).

As has been noted above, the investigation of the southern foci shows that there is a connection between wild and domestic rodents there with the existence of a common flea, Ceratophyllus (Nosopsylla) nicanus. Nevertheless, at present there are no data permitting us to claim the possibility of existence of such a mechanism of occurrence of plague among domestic rodents with subsequent infection of people, as is observed in Northeast China, in the southern provinces of the Chinese People's Republic (Fukien, Kwangtung, Szechwan and Shensi). However, the epizootiological material obtained make us consider carrying out appropriate research work, that is, a search for plague in wild nature, absolutely essential. Plague stations existing in these provinces are concentrating their scientific activity specifically along this line.

We should not overlook the fact that the study of the natural focalization of plague from this aspect on our territory is beginning to interest Indian investigators. These investigations are undoubtedly interesting for solving the problem of the primary natural localization of plague in the southern provinces of the Chinese People's Republic. This interest is determined to a certain degree by the analogy of the rodent fauna and of the nature of the geographic landscape in the southern provinces of China to adjacent territories of the republics of India and Burma.

Of entirely independent interest is the search for plague foci on the territory of Tibet and the northwestern portion of the province of Szechwan. Their geographic landscape and fauna permit us to express the idea of the possibility of the existence of a natural focus of plague here also. The prospects outlined in doing research work on these territories are making it possible to solve this problem.

Dealing with the prospects of scientific research work on plague it should be noted that the study of the problem of natural plague focalization on the territory of the Chinese People's Republic is certainly not limited to doing epidemiological investigations directed at a search for new foci and detection of acute epizootics.

Study of the rules and regulations of existence of the natural focalization of plague and, particularly, of the ecologico-physiological characteristics of components of plague foci in different geographic landscapes is basic for practical measures on the elimination of the foci and will serve as obligatory topics for scientific research work by plague institutions of the Chinese People's Republic. In addition to this, in the topics of scientific works special attention has been directed to the development of problems of prophylaxis: specific vaccination, search for new methods of rodent control and control of their ectoparasites, etc.

As has been noted above, the main obstacle to developing measures on plague is the absence of native specialist cadres. In connection with this, appropriate training of young specialists from the group of those being graduated from higher institutions of learning and advanced training for existing cadres of pestologists is becoming a problem of current importance for the Ministry of Health of the Chinese People's

Republic and its Institute of Epidemiology and Bacteriology. With this aim in view, in 1957-1958 plans were made to organize appropriate courses.

It should be noted that cadres of epidemiologists not only in a limited specialty but also of a general category are very insufficient in the Republic. Incidentally, their qualifications differ extremely. This situation interferes with the solution of a whole series of general epidemiological problems confronting workers in sanitary-epidemiological stations and the epidemiological departments of the institutes of vaccines and sera.

All this made it necessary at the end of last year, 1956, to organize as an emergency four-month courses for the advanced training of epidemiologists with broad specialization at the Institute of Epidemiology of the Ministry of Health of the Chinese People's Republic. It should be said that with the organization of these courses, essentially the basis was laid for a system of advanced training of epidemiologists in the Chinese People's Republic. The courses are given by a group of scientific workers of the Institute of Epidemiology and Bacteriology with the participation of a Soviet specialist, V. V. Shunayev, bringing in great Chinese scientists from Peking, Shanghai and other cities for giving lectures on various problems of specific epidemiology.

We cannot help by emphasize a certain characteristic feature of these courses. It consists of the fact that considerable attention in their program has been given to the solution of tactical problems on various matters of epidemiology. The specific epidemiological situation at the place of work of each student constitutes the basis of these problems. Appropriate materials were used by each student while traveling to the courses.

The solutions of the tactical problems are given in the form of reports at gatherings of students and teachers, where they are discussed with an appropriate conclusion by the leader of the assignment. This characteristic of the course program will assist in obtaining epidemiologists with a good theoretical training and definite practical experience.

In conclusion, I should like to say that the problem posed by the CP and the government of China on the elimination of plague in China is a very important one, constituting one of the most important tasks in the field of public health. We are sure that it will be solved. Thereby, we are hoping for the continuation of assistance from the Soviet Union with its exceptionally rich experience in the matter of solving problems of eliminating natural plague foci.

pp 114-116

Progress in the Control of Plague in the Chinese People's Republic

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During the 40 years of existence of the Soviet regime Soviet public health has made brilliant progress in the control of plague-- it has completely eliminated the epidemic form of this dangerous disease in the Soviet Union, which previously killed a considerable number of people.

Soviet scientists, utilising the world-wide antiepidemic experience, accumulated much of its own experience in the field of epidemiology, bacteriology, medical zoology, parasitology, immunology, disinfection, and the production of bacterials. In creatively developing the science of the control of plague they have enriched this science with new knowledge, which will give us the possibility of combating this scourge of mankind even better.

In old China, during the rule of the reactionary government, plague epidemics were not uncommon. From the northeastern boundaries of the country to the Leichoupantao peninsula in the south of China, from the eastern provinces of Szechwan and Fukien to western Sinkiang-Uigurian Autonomous Oblast there were more than 10 foci of plague epidemics. In these difficult times tens of thousands of people died of plague. There are old verses in Chinese which indicate how dangerous plague epidemics were in old China:

> Rats died in the East
> and died in the West.
> People feared the dead rats like tigers.
> Several days after the death of the rats
> Walls were formed of the bodies of the dead people,
> People died night and day.
> The number of dead was hard to count.
> People did not see the bright sunshine
> because of their depressed state.
> Of three who went down the road,
> Two died before going ten paces.

At the beginning of the People's Freedom War, during the difficult years of the people's revolution Japanese criminals blew up a base where agents were being prepared for bacteriological warfare which was located in the northeast of the country in the locality of Ping-Fang, thereby causing serious plague epidemics. At that time, medical workers of the People's Freedom Army still did not have experience in controlling this disease; they had no special knowledge nor the most essential equipment;

in the country there was a shortage of plague workers.

Beginning with 1947, the Ministry of Health of the Soviet Union has assisted in eliminating plague in China, which claimed about 10,000 human lives, by repeatedly sending plague detachments to China; this aid assisted us in winning the revolution.

During the first few days of existence of the Chinese People's Republic, in 1949, when plague again broke out in the locality of Chahar the Ministry of Health of the Soviet Union responded to the request of our government again, giving us great assistance by sending plague detachments headed by Professor I. I. Rogozin, corresponding member of the Academy of Medical Sciences of the USSR, and Professor I. N. Mayskiy. These detachments assisted us in eliminating the epidemic which had begun in the northern part of the Chahar province, and by the same token eliminated the danger of importation of plague into the heart of China-Peking. This not only saved the lives and health of many Chinese, but also maintained the authority of the people's government.

As a result of such expeditionary assistance, the Chinese antiepidemic service developed rapidly; in addition, we obtained constant aid from Soviet specialists working for longer periods in the Chinese People's Republic. Therefore, despite the use of bacteriological weapons against China in 1952 in the northeast of our country by American war criminals our antiepidemic services were able to eliminate the danger of spread of infectious diseases rapidly. The Soviet antiepidemic delegation which came to China in 1955 headed by B. N. Pastukhov, after thoroughly investigating Chinese antiepidemic work, gave considerable valuable advice. Soviet consultants and advisors who worked in China certainly played a great part in the control of plague in recent years.

Because of the disinterested aid of the Soviet people, proper supervision of the Chinese government, conscientious work of Chinese antiepidemic workers and support by the people we were able to liquidate plague epidemics among the people. We succeeded in doing so by borrowing from Soviet progressive experience on plague control in the USSR— comprehensiveness in measures taken, which we developed in accordance with our own specific conditions.

I should like to present certain figures: if the plague morbidity rate in 1950 is assumed to be 100, then in 1951 it decreased to 54.7 percent; in 1952, to 23.8 percent; in 1953, to 10 percent; in 1954, to five percent; in 1955, 0.8 percent; in 1956, in all of China there were only two cases of plague. Previously, the number of patients cured of plague amounted to 20-30 percent, and beginning with 1953 this number increased to 97.8 percent. Plague was not found among people for the following periods: for six years in the province of Szechwan and in the locality of Chahar; for five years, in the provinces of Shansi and Kwangtung; for four years, in the former province of Jehe; for one year, in the autonomous region of Inner Mongolia. Despite the existence of more than 10 natural foci of plague in the country, in 1956 there was only one case of plague in the canton of Kangtsa in the province of Tsinghai and one case in the canton of Zang-yü in Kirin Province.

Now, it may be stated that the possibility of occurrence of cases of plague among the people has been considerably reduced, but we know that we cannot be satisfied with this, because in recent years places have been detected where epizootics are still being observed among rodents. Thus, in Kirin Province there are four such places; in the environs of Harbin, five; in the Sinkiang-Uigurian Autonomous region, two in the province of Tsinghai, three; in the autonomous region of Inner Mongolia, 34. In all these places plague institutions have been organized which are taking the necessary plague measures.

Our progress is evidence of the effectiveness of Soviet plague measures. At the present time, in China there are quite a few plague workers trained by Soviet specialists. These workers, who worked in cooperation with Soviet specialists ten years ago have become China's main strength and support in the control of plague.

In communicating this information I cannot help but express gratitude to the Soviet Union in the name of all antiepidemic workers and the people of China for the great disinterested assistance given to us by Soviet specialists!

pp 181-187

Current Status of the Problem of the Role of Ticks of the Superfamily Ixodoidea in the Natural Focalization and Epizootology of Plague

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Aside from fleas, the role of which in the natural focalization of plague has already been determined, in almost all foci of plague during epizootics the infection of ticks is observed with the plague microbe which frequently reaches a high degree. However, to date the actual significance of ticks as vectors and reservoirs of the plague microbe is not clear.

In 1911, I. I. Mechnikov, during his visit to Astrakhanskiy Kray, expressed the idea that "the vectors of the infection (that is, of the plague microbes A. and M.) must be considered the ticks encountered behind the ears of sousliks". In 1928, A. M. Skorodumov isolated a culture of the plague pathogen for the first time from a tick taken from a tarbagan in the Transbaikal. The species of tick remained undetermined but it was most likely Ixodes crenulatus. Later, M. M. Tikhomirova and S. M. Nikanorov (1930) isolated a culture of the plague microbe from eight specimens of Rhipicephalus schulzei taken from a souslik found in the steppe which died of plague.

At the same time, D. A. Golov and A. N. Knyazevskiy (1930) found a culture of the plague pathogen in R. schulzei ticks which had been collected in an empty souslik nest, probably several weeks after the death of the latter from plague. At the same time, M. M. Tikhomirova and S. M. Nikanorov (1930) reported isolating a plague culture from three Ixodes crenulatus ticks taken from an experimentally infected tarbagan.

The findings of infected ticks in nature caused D. A. Golov and A. N. Knyazevskiy, M. M. Tikhomirova and S. M. Nikanorov, D. N. Zasukhin, V. V. Suknev and other investigators who expressed the idea that ticks, by virtue of their ecological characteristics, are more reliable reservoirs and vectors of the plague microbe than fleas and may be of epizootological and epidemiological significance. At the same time, the findings of infected ticks served as an impetus to performing experimental work which had the aim of determining the part played by ticks as reservoirs and in transmitting the plague microbe. T. D. Fadeyeva (1932), in experiments with Argas persicus ticks, determined the susceptibility of this species to plague and the ability of all developmental stages to preserve the plague microbe up to 110 days. A. K. Dyuzenkov and G. D. Donskov (1933) determined the fact that Hyalomma scupense ticks take up and preserve in their bodies virulent plague microbes after feeding on experimentally infected animals; thereby, the adult ticks preserve these microbes up to 11 days; the nymphs, up to three days; the larvae, seven days. In addition, by means of interrupted feeding of ticks taken from infected animals after being half fed and placed on healthy animals

these authors brought about the transmission of the plague microbe and infection of sousliks with plague. In this series of experiments the plague microbe was isolated from tick excrement.

D. N. Zasukhin (1930) and then D. N. Zasukhin and M. M. Tikhomirova (1936), in similar experiments with Dermacentor marginatus ticks, noted the preservation of the plague microbe in the larvae of ticks up to 10 days and in the nymphs up to six days after feeding them on experimentally infected hamsters.

These first attempts at clarifying the epizootological role of ixodial ticks under experimental conditions could not throw light on the significance of ticks in the preservation and transmission of the plague microbe in connection with the fact that ticks which did not have any biocoenotic relations with the main or secondary reservoirs of plague were used in the experiment. Subsequently, with the extension of investigation of natural plague foci, Hyalomma asiaticum asiaticum, Haemaphysalis numidiana turanica, Rhipicephalus pumilio, Rh. schulzei, Ixodes crenulatus, I. persulcatus, and Ornithodorus tartakovskyi ticks were found in nature infected with plague.

It is important to emphasize that all these tick species have close biocoenotic relations with rodents-- the main plague vectors in nature. Whereby, two species are of particular interest: H. asiaticum asiaticum and O. tartakovskyi, biocoenotically related to jirds but also parasitic on camels. This circumstance permits us to suppose the possibility of transmission of plague infection by ticks of these species from jirds to camels and back.

In subsequent years the role of ixodial and argasid ticks was studied in an intensified manner under experimental conditions and in nature by many investigators: N. D. Yemel'yanova (1950), O. V. Afanas'yeva, T. A. Burlackenko and V. V. Shunayov (1948-1951, manuscript); N. D. Yemel'yanova (1950), N. D. Yemel'yanova and A. V. Karatayeva (1953), K. I. Kondrashkina (1957), T. A. Burlachenko (1956), O. V. Afanas'yeva and I. F. Volosivtsov (1956, manuscript). In these works a study was made of ticks which were in close biocoenotic relation with the main plague reservoirs in nature-- I. crenulatus, R. schulzei, H. asiaticum asiaticum and O. tartakovskyi.

As a result of these studies a high degree of susceptibility of all stages of tick development to the plague microbe was determined. The number of infected ticks in different experiments varied within broad limits, sometimes reaching 100 percent, whereby it was made clear that the success of the infecting feeding depends on the proper selection of the host, on the specificity of the ticks for the host, and the nature of the course of the infectious process with experimental infection of the animal (the time of occurrence and the duration of bacteriemia).

For all the species of ticks studied the possibility was determined of prolonged preservation of the plague pathogen in their bodies. Thus, K. I. Kondrashkina, V. A. Merlin and Z. A. Obukhova (1951, manuscript) caused the preservation of the plague microbe in the bodies of R. schulzei for 43 days in experiments. O. V. Afanas'yeva (1956) maintained the

plague microbe in female I. crenulatus ticks up to 500 days; in the nymphs, up to 203 days. N. D. Yemel'yanova and A. V. Karatayeva (1953) determined the preservation of the plague microbe in the larvae of I. crenulatus for 155 days.

T. A. Burlachenko (1956) noted that although the main mass of O. tartakovskyi ticks is rapidly freed of microbes after experimental infection with plague, in various individuals the plague microbe remains up to 171 days. O. V. Afanas'yeva and I. F. Voloshivtsev (1956) determined the fact that the plague pathogen was preserved in female H. asiaticum asiaticum for 133 days (this was not the maximum time).

In addition to the facts indicated above, accumulated during the course of experimental research on the duration of survival of the plague microbe in the bodies of ticks, a number of authors expressed certain considerations on this subject as a result of their observations in nature. Thus, K. I. Kondrashkina (1957), on the basis of finding an apparently unfed R. schulzei female tick infected with plague in nature early in the spring (May), came to the conclusion that this female tick could have been infected while still in the nymph stage in the previous year, that is, no less than 9.5 months before it was subjected to bacteriological examination. O. V. Afanas'yeva, T. A. Burlachenko and V. V. Shunyov (1948-1951, manuscript), who observed a plague epizootic among marmots in Tien Shan and who found ticks in all stages of metamorphosis in nature infected with plague, came to the conclusion that I. crenulatus ticks are capable of preserving the plague microbes in their bodies for an entire developmental cycle, that is, no less than three years.

A number of investigators studied the problem of the possibility of transmission of the plague microbe from one stage of development to the next in the course of metamorphosis. K. I. Kondrashkina and co-authors brought about the transmission of the plague microbe from the larvae to the nymphs and separately from the nymphs to the adult ticks of R. schulzei. N. D. Yemel'yanova and A. V. Karatayeva observed the passage of the plague microbe from the larvae to the nymphs of I. crenulatus ticks during the course of metamorphosis. T. A. Burlachenko determined the possibility of transmission of plague from one nymph phase to the next for O. tartakovskyi. No transmission from stage to stage was produced.

The data listed exhaust those accumulated experimentally at the present time concerning the interstage transmission of the plague microbe in ticks. At the same time, the findings of ticks infected with plague in nature, which ticks were apparently unfed in the nymph and imago stages of I. crenulatus (O. V. Afanas'yeva) and in the nymph and imago stages of R. schulzei (K. I. Kondrashkina) are taken as facts of the indisputable proof of the existence of interstage transmission of the plague pathogen in ticks in nature.

Some investigators have studied the problem of the possibility of transovarial transmission of the plague microbe. It has been proved that in the clutches of eggs of certain female I. crenulatus ticks

infected with plague the plague pathogen was maintained in a viable state up to 107 days (Afanas'yeva, 1956). The existence of the plague microbe among the eggs of I. crenulatus was also determined by N. D. Yemel'yanova and A. V. Karatayeva (1953). At the same time, not a single one of the larvae which hatched from these eggs was infected with plague. Despite the failure of attempts to prove the existence of actual transovarial transmission of the plague microbe in ticks experimentally, some authors believe in their works that such transmission exists in nature. In their opinion, findings of infected unfed larvae in nature serve as the basis for such a conclusion. Thus, for example, unfed larvae infected with plague under natural conditions in the case of I. crenulatus ticks have been found in Tien Shan by O. V. Afanas'yeva.

A study was also made of the problem of the possibility of active transmission of plague pathogen by ticks from a sick to a healthy animal. Such transmission could be accomplished by A. K. Borzenkov and G. D. Donskov (1933), but only under condition of interrupted feeding of H. asiaticum ticks taken half-fed from infected hosts and transplanted to healthy dwarf sousliks. K. I. Kondrashkina, V. A. Merlin and Z. A. Obukhova (1948-1951, manuscript), repeating the experiment by A. K. Borzenkov and G. D. Donskov with half-fed R. schulzei ticks on infected dwarf sousliks did not obtain clear-cut results. Although it was possible to infect the healthy sousliks with plague the authors did not find any of the infected ticks transplanted on two sousliks which died of plague. In this case, the possibility has not been ruled out that the sousliks which died were infected either by means of eating the infected ticks or, as the authors suppose, by contamination, that is, by rubbing in the infectious excrement or contents of the internal organs of crushed ticks.

In the case of O. tartakovskyi, T. A. Burlachenko proved the possibility of plague infection of healthy test animals by means of an infected tick bite if the tick had been removed from an animal sick with plague no longer than three days before being transplanted to the healthy animal. Thereby, it was impossible to produce infection of the rodent after longer periods or by a tick which had undergone metamorphosis after the infecting feeding.

A case of experimental infection of a camel with plague by O. tartakovskyi ticks (T. A. Burlachenko, manuscript) deserves attention, but in this case the possibility has not been ruled out that the camel was not infected by the tick bite but rather by some other method, because part of the ticks had been crushed by the camel during the experiment. As is seen from what has been presented above, the possibility of transmission of the plague pathogen by the bite of infected ticks during interrupted feeding should be regarded, most likely, as a mechanical transfer of the infectious principle from a sick to a healthy animal.

These, in general outlines, are the factual materials accumulated at the present time on the problem of the possible epizootological significance of ticks. Let us now proceed with the analysis of this material. As is seen from the material presented above, at present it may be considered proved beyond doubt that: a) ticks of different species

can be infected with the plague pathogen experimentally and in nature, whereby the percentage of ticks infected may be very high; b) there is a possibility of prolonged preservation of the plague microbe in the bodies of ticks; c) there is a possibility of transmission of the plague microbe by ticks from one developmental stage to the next; d) there is a possibility of infection of a healthy rodent with plague by means of a bite of an ixodial tick during interrupted feeding as well as by the bite of an argasid tick at the time of a second feeding in the same developmental stage in a period of no more than three days after the infecting feeding of the tick.

The possibility of infection of a rodent with plague after chewing on an infected tick and subsequently eating it or rubbing its excrement and the contents of its organs into the skin may be considered indirectly proved (K. I. Kondrashkina, V. A. Merlin and Z. A. Chudhova, O. V. Afanas'yeva and others). As for transovarial transmission of the plague microbe in ticks, this can be determined reliably only under experimental conditions.

It should be emphasized that to date none of the investigators has been able to produce infection of a healthy rodent with a tick which has undergone metamorphosis after an infecting feeding. It is important to direct attention also to the fact that despite the high degree of infectiousness of the ticks themselves, all cases in which it was possible to infect a rodent with a tick-- an ixodial tick during interrupted feeding or an argasid tick at the time of a second feeding-- represent isolated cases in a large number of experiments performed. Thus, for example, in the experiments of K. I. Kondrashkina, V. A. Merlin and Z. A. Chudhova R. schulzei ticks were 49.4 percent infected when they fed on sousliks sick with plague; when half-fed ticks finished their meals on healthy sousliks it was possible to produce the plague infection in only two out of 12 sousliks, although in total 550 ticks which had been half-fed on plague-infected sousliks before this had finished their feeding on these 12 sousliks. The same authors, attaching 778 ticks first half-fed on sick animals to 20 guinea pigs, were unable to produce a single case of plague infection of a healthy guinea pig, although the infection in the ticks themselves reached 10 percent in this experiment. T. A. Burlachenko produced a plague infection in only seven sousliks out of 49 by a second feeding of the O. tartakovskyi ticks on healthy animals one-two days after the infecting feeding, although in her experiments from 10 to 100 ticks fed a second time on each animal, and infection in those ticks amounted to 98 percent during the first two days after the infecting feeding.

The mechanism of transmission of the plague pathogen to healthy animals in those few cases where such transmission could be accomplished also remains unclarified. To date, the problem of whether the microbes of plague simply survive in the tick organism or whether those microbes are capable of multiplying in the tick digestive tract has not at all been clarified either.

Finally, the effect of a stay in the tick organism on the basic

properties of microbes, particularly on their virulence, remains unclear. Opinions of investigators differ on this subject: while N. D. Yemel'yanova, A. V. Karatayeva and V. V. Shmeyev note a high degree of virulence in plague microbe strains isolated from ticks, the materials of L. M. Osadchaya (1957) show the instability of such strains and indicate that when those strains are kept in a museum their virulence weakens more often and more rapidly than that of strains obtained from fleas or rodents sick with the acute forms of plague.

An analysis of materials existing at the present time leads to the conclusion that ixodial and argasid ticks cannot be of essential importance in the development of epizootics, that is, in the extensive spread of the plague pathogen among the rodent population.

With respect to ixodial ticks this conclusion is substantiated by the extreme difficulty and perhaps the impossibility of transmitting the plague microbe to a healthy animal by means of the bite of a tick which has undergone metamorphosis. The transmission of the pathogen during interrupted feeding, which is more or less haphazard, cannot be regular and frequent in nature. Even if we assume the possibility of plague transmission by ticks which have undergone metamorphosis after infection, the biological characteristics of ixodial ticks-- their prolonged developmental cycle, feeding (normally) once during each stage of development-- exclude the possibility of rapid and extensive spread of the plague pathogen by ticks among rodents even if we make this assumption.

For O. tartakovskyi argasid ticks which are fed a second time in each stage, T. A. Burlachenko determined the fact that the majority of infected ticks eliminates the microbe in a period of one-one and a half months after the infecting feeding, while transmission of the microbe to healthy animals is possible only during the first three days after infection of the ticks. Both Russian investigators (Fedorov, Rogozin, Fenyuk, 1955 and others) and foreign investigators (Pollitzer, 1954, Nuttal and others) have come to the conclusion that ixodial and argasid ticks cannot play an essential part in the development of plague epizootics.

At the same time, the idea cannot be ruled out that the duration of preservation of plague in the tick organism, at least in part of the tick population, the possibility of interstage and possibly transovarial transmission and subsequent infection of healthy rodents, if not by bite then by chewing or crushing the ticks, can account for the significance of ticks in the carriage of infection through the so-called "interepizootic periods" and in the occurrence after that of the first cases of disease among rodents in new and, as a whole, less immune rodent population.

Thus, K. I. Kondrashkina (manuscript) points out with respect to one epizootic that the "beginning of the spring epizootic did not coincide with the awakening of sousliks from their winter sleep or with the period of the highest census of Neopsylla setosa fleas nor with the beginning of colonization of young sousliks. It coincided with the mass spring parasitization of R. schulzei ticks on sousliks". The author concludes that "ticks not only carried the plague infection through the

6964

winter interepizootic period but also were the causes of occurrence of epizootics among dwarf souslik populations". N. D. Yemel'yanova (19__) points out that in the Transbaikal mass spring-summer tick infestation of tarbagans with I. crenulatus ticks not uncommonly coincided with the onset of a plague epizootic in the tarbagans. However, we cannot help but emphasize that conclusions concerning the possible role of argasid and ixodial ticks in the long preservation of the plague pathogen and carriage of it through the interepizootic periods are derived simply from indirect considerations and so far have not been convincingly proved by anyone either experimentally or under natural conditions.

In conclusion, we should like to note that for more complete elucidation of the epizootological role of ticks in plague, it is important to direct attention of investigators chiefly to the solution of the following problems: a) careful checking of the possibility of transmission of the plague pathogen to a healthy rodent by a tick which has undergone metamorphosis after an infecting feeding; b) checking of the possibility of creation of an experimental epizootic in a group of susceptible rodents under conditions where other vectors, aside from ticks, have been excluded (according to a system similar to the experiments of the Indian commission on fleas); c) study of the mechanism of transmission of the plague pathogen by ticks after a bite and other methods of infection; d) elucidation of the fate of the plague microbe in the bodies of ticks; e) planned and directed search for ticks infected with plague in natural foci during interepizootic periods and study of the conditions of carriage of the pathogen by the ticks from one epizootic period to the next.

From everything presented the following main conclusions can be drawn: 1. the epizootological significance of ticks in plague has been inadequately studied, since a number of important questions remain unanswered. 2. existing materials permit us to conclude that ixodial and argasid ticks cannot be of essential importance in the development of epizootics. 3. it may be assumed that ixodial and argasid ticks can be one of the factors providing for the carriage of plague through inter-epizootic periods lasting many years; however, this idea needs factual confirmation by experiments and observations in nature. 4. study of the epizootological significance of ticks in plague should be continued, and special attention should be paid to the study of the part played by ticks in the long maintenance of the natural focalization of plague and study of the fate of the plague microbe in the tick organism.

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pp 337-344

Problems of the Pathogenesis, Therapy, Vaccine Prophylaxis and Diagnosis of Plague

Characteristics of the Pathogenesis of Primary Pneumonic Plague and their Epidemiological Significance

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Introduction

The problem of the mechanism of occurrence of primary pneumonic plague remains controversial to date. There is no adequate concept in existence concerning the dynamics of the development of this disease, and there are no ideas which would be scientifically substantiated to the proper degree concerning the infectiousness of pneumonic plague for persons around the patient in one period or another of the development of his disease.

The majority of authors studying outbreaks of pneumonic plague and its pathogenesis are inclined to believe that plague pneumonia is an independent form of the disease in which from the very onset pulmonary symptoms are predominant. This form of disease occurs by inhaling air infected with plague microbes, that is, the infection occurs aerogenically. At the same time, to date there is no agreement on the question of how the plague pathogen penetrates into the pulmonary tissue in a droplet infection.

Some investigators, for example, S. G. Kulesha (1911), and N. N. Klodnitskiy (1911, 1913) and others believe that the plague microbes do not penetrate immediately into the pulmonary tissue with the inhaled air but rather first settle on the tonsils and mucosae of the nasopharynx and trachea. Here, in the opinion of these investigators, an inflammatory process develops which leads to the formation of necrosis, as a result of which the mass of plague microbes, "proliferating through" the capillary and vein walls, penetrates into the blood and is carried into the lung tissue. These authors base their conclusions on the fact that changes in the tonsils and tracheal mucosa should be considered the first plague lesions in pneumonic plague by virtue of their quantitative and qualitative changes. Therefore, pneumonic plague, in their opinion, is a secondary phenomenon (hematogenous).

Other authors-- N. M. Kolesnikov (1932), S. I. Potin (1914), Wu Lien-tieh (1926), V. K. Vysokovich (1897), P. P. Zabolotnov and B. N. Shmidt (1930) and others, also based on the study of pathological changes in human organs and those of experimental animals which died of pneumonic plague, believe that in this form of the disease the primary changes

develop from the very onset directly in the lung tissue (bronchioles, alveoli). In their opinion, plague microbes penetrate immediately into the bronchioles and alveoli along with the inhaled air, as a result of which primary plague pneumonia occurs.

Such opposite conclusions, in our opinion, were the result of the fact that investigators studied cadaver material which could not give the correct idea of the dynamics of the infectious process in the pneumonic form of plague. Cadaver material gives us an idea only of the end stage of the process which produces severe lesions in the entire body (including the tonsils and the trachea); experiments on the reproduction of pneumonic plague in laboratory animals were performed with primitive equipment and on a small number of animals.

In order to understand correctly the developmental dynamics of primary pneumonic plague it is necessary to observe at least two conditions: 1) the observations of the development of the infectious process should be made methodically from the beginning of its occurrence (that is, from the time of infection) until the death of the organism; such experiments can only be conducted on animals, but on quite large numbers of them. 2) infection of experimental animals (guinea pigs are best) should be carried out only by the inhalation method, which is closest to the natural route of infection-- the aerogenic route.

The experiments being described below, which are part of the works which we carried out under the direction of Professor V. N. Fedorov, show in all evidence that the inhalation method of infection is the best for reproducing the picture of primary pneumonic plague in guinea pigs.

Method of Work

Guinea pigs weighing 300 to 400 grams were infected aerogenically with a virulent plague microbe culture. For this purpose, they were placed in groups of 20 in a chamber of the inhalation apparatus for 30 minutes which was specially constructed at the "Mikrob" Institute. An aerosol made of a plague microbe culture was also introduced into the chamber.

At different periods after infection with the aerosol culture, specifically after 10 minutes, one hour, two, three-six, 12, 24, 36, 48, 60 and 72 hours, we killed three-four guinea pigs at a time and subjected their organs to a careful bacteriological study. From each guinea pig 19 cultures of different tissues and organs were made. Bacterial cultures were made from the following: conjunctiva, cervical, submaxillary and supraclavicular lymph nodes, tonsils, the bone marrow of the sternum and vertebra, the tracheal mucosa, lymph nodes at the tracheal bifurcation, lungs, heart muscle, blood, liver, spleen, kidneys, suprarenal glands, nasal mucosa and nasal sinuses. The cultures were made on blood agar only. These organs and tissues were fixed simultaneously in 70 percent alcohol and 10 percent formalin solution for subsequent histologic examination.

Results of Experiments

In all, in our experiments 39 guinea pigs were infected by the inhalation method. During their stay in the chamber (30 minutes) 1,000,000,000 microbes of a two-day agar culture of the plague microbe were sprayed into the chamber, the CLD of which was equal to 100 microbes for guinea pigs by subcutaneous injection.

After infection of the guinea pigs they were placed in 10-liter jars and were killed and examined after definite periods of time. The general results of the bacteriological investigation of the guinea pigs are shown in Fig. 1.

As the result of autopsy, bacteriological and histological examination of the organs and tissues of guinea pigs results were obtained which give us quite a distinct picture of the development of the infectious process.

1. During the first three hours after infection no visible macroscopic changes could be noted in the organs and tissues of the guinea pigs.

Histopathological study of them showed the occurrence of an accumulation of neutrophiles in the lumina of the blood vessels of the nasal mucosa and mucosa of the accessory sinuses and in the lumina of the tracheal blood vessels. In guinea pigs killed after three hours, scattered hemorrhages were found in the lungs.

At the same time, even in the first few minutes after infection the plague microbe was cultured from the mucous membranes of the upper respiratory tract and from the lungs. Thereby, the culture was grown not only from areas of the lungs located in the vicinity of the large bronchi, but also from distant areas (lateral area). True, the culture grew in the form of scattered colonies from these areas, while in cultures from the tracheal mucosa growth was more abundant. This is evidence that after inhalation of aerosols by the animals the microbes not only settled on the mucous membranes of the upper respiratory tract, but also penetrated deeply into the lung tissue in all its lobes. This was confirmed in a particularly clear-cut manner by isolation of the culture from lung tissues of guinea pigs killed in the first few minutes after the infection.

2. On investigation of guinea pigs killed 6-12 hours after infection a certain enlargement of the cervical and bifurcation lymph nodes was noted as well as the existence of small foci of congestion in the lungs. On histological examination nonpurulent inflammatory infiltrates were found in the tracheal mucosa of such guinea pigs. In the peritracheal tissue foci of serous inflammation with hemorrhages were noted. Small hemorrhages were encountered in the lungs. Subsequently (after 12 hours) microscopic foci of catarrhal-hemorrhagic pneumonia appeared, and hyperplasia of the cervical and supraclavicular lymph nodes and of the reticular cells of the spleen was also noted.

Fig. 1. Results of Bacteriological Examination of Guinea Pigs Infected by Inhalation of a Plague Microbe Culture. The results obtained for individual animals are separated by fine horizontal lines. 1. time of culture after infection; 2. mucous membranes; 3. of the nose; 4. of the trachea; 5. tonsils; 6. lungs; 7. lateral area; 8. apex; 9. medial area; 10. lymph nodes at bifurcation; 11. spleen; 12. blood; 13. liver; 14. kidney; 15. suprarenal glands; 16. cervical lymph nodes; 17. minutes; 18. hours.

Despite the existence of these changes the plague microbe culture could be obtained from only two guinea pigs out of seven: from one it was obtained from the nasal mucosa; from the other, from the mucosa of the nasal sinuses. Instead of the increase in the frequency with which the plague microbe could be plated out of the guinea pig organs expected a reduction was noted which created the impression that the microbes had disappeared from the lung tissues and from the mucous membranes of the upper respiratory tract. Such a "latent" (in a bacteriological respect) period of infection apparently is explained by the existence of some protective processes in the guinea pig organism, which temporarily prevent detection of the plague microbe culture in such early periods after infection.

3. In guinea pigs killed 24 hours after infection, definite inflammatory signs were found in the cervical lymph nodes and particularly in the lungs. In the lungs the foci of densification were large and at

times included almost entire lobes of the lung.

The plague microbe culture was isolated only from lung tissue. On histologic examination of the organs of these guinea pigs changes were noted which were the same as in guinea pigs killed 6-12 hours after infection, with the difference only that foci of pneumonia were encountered in them more often and they were larger. In addition, in one case a cervical bubo was found with areas of necrosis, hemorrhages and a serous-hemorrhagic exudate in the tissues surrounding the bubo. These changes in the lungs are evidence of the existence of a typical plague pneumonia in the guinea pigs.

4. In guinea pigs killed 36 hours after infection further spread of the pneumonic foci was noted. The changes in the lymph nodes remained approximately the same as previously.

On histologic examination the following were found: extensive accumulation of neutrophiles in the lumina of the nasal mucosal blood vessels, its accessory sinuses, and the trachea. In the submucosa of the nose and accessory sinuses there was an infiltration with histiocytes and lymphoid cells. In the lungs there was catarrhal and catarrhal-purulent pneumonia.

The culture of the plague microbe was isolated not only from the lung tissue and from the tissue of the lymph nodes but also from the tissue of the spleen, although changes could not be found in it. This indicates the penetration of plague microbes from primary foci of specific inflammation in the blood and their spread throughout the entire body (bacteriemia).

5. In guinea pigs investigated 48 hours after infection extensive lesions were noted in the lungs including many lobes. Areas of periadenitis were superimposed on the changes in the lymph nodes of these guinea pigs. In the spleen and in the liver no apparent changes could be found. The mucous membrane of the trachea (one case) was covered with a white coat.

On histologic study of guinea pig organs in this group focal hemorrhage was noted (one case) along with the maintenance of a large number of neutrophiles in the lumina of the blood vessels of the nasal mucosa and accessory sinuses. In the trachea there were foci of catarrhal inflammation and necrosis. In the lungs foci of pneumonia were found: in one case, focal catarrhal and catarrhal-purulent pneumonia; in an other, confluent serous-hemorrhagic and catarrhal pneumonia; in still another, confluent catarrhal-hemorrhagic and catarrhal pneumonia with multiple hemorrhages under the pleura.

A plague microbe culture was isolated from all organs and tissues, including the spleen, liver and blood. Such pathological changes and the results of bacteriological investigation were evidence of generalization of the process.

6. Afterwards (after 60-72 hours) pathological changes in the lungs and other organs were more widespread and more intense. The basic specific changes at this time were concentrated in the lungs. Lymph nodes were also inflamed, but areas of periadenitis were absent from some of

them. The tracheal mucosa was covered with a mucous or bloody coat, and a serous fluid exuded from the nasal cavity. The liver and spleen remained without visible macroscopic changes.

According to the data of histologic study of the organs it is seen that numerous areas of confluent serous and catarrhal-hemorrhagic pneumonia developed with an abundant accumulation of plague microbes in the alveoli, blood vessels, capillaries and interstitial tissue. In the nasal mucosa and the mucosa of the accessory sinuses congestion was observed with cellular infiltration (macrophages, leucocytes, lymphoid cells). Accumulations of plague microbes were found among the necrotic masses which had separated from the nasal and tracheal mucosae.

The plague microbe culture was isolated from all organs and tissues and the mucous membranes of the upper respiratory tract; the growth of the culture in all cases was a confluent one.

Discussion of Experimental Data

An analysis of all the data which we obtained, described schematically in the previous section, permits us to make a number of generalizations. The fact attracts attention that not all the lymph nodes were affected simultaneously. Whereas in the lymph nodes at the tracheal bifurcation adenitis and periadenitis were noted in the early periods after infection, the cervical, submaxillary and supraclavicular nodes were not always involved and, were affected chiefly in the late periods of the disease. These lesions developed initially without periadenitis, and only after 48-72 hours were all the elements of the plague bubo observed in them.

It should also be noted that the plague microbe culture was isolated in the form of scattered colonies from the mucous membrane of the upper respiratory tract during the first three hours after the infection.

Subsequently, in periods up to 24 hours, it was isolated in only two out of seven cases from the nasal mucosa and from its accessory sinuses. During the period from 24 to 36 hours the culture was not isolated at all. Only after pneumonic foci appeared in the lungs and the infectious process took on a generalized form and the mucous membranes of the upper respiratory tract were covered with a purulent or purulent-hemorrhagic coat rich in plague microbes did the culture begin to be isolated constantly and abundantly, as occurred in the last hours of the disease.

The coat on the mucous membrane of the upper respiratory tract was apparently made up of phlegm exuded from the pneumonic foci. Therefore, a secondary dissemination of the plague bacillus occurred over the mucous membranes of the upper respiratory tract with a marked increase of inflammatory phenomena in them.

The observations made permitted us to understand the mechanism of occurrence of primary pneumonic plague, and succeeded in establishing the site of the primary localization of the plague microbe by the inhalation method of infection of guinea pigs and determined the possible nature and routes of excretion of the plague microbe from the sick organism.

Plague microbes, after inhalation infection (by the droplet route) passing through the upper respiratory tract, settle on the mucous membrane (larger aerosol particles) and the small particles of the aerosol penetrate into the deep areas of lung tissue. In the site of localization of plague microbes inflammatory phenomena occur, in which to varying degrees the local (regional) lymph nodes are involved.

In lung tissue pneumonic foci of the lobular or confluent pneumonic types develop rapidly. The development of the foci in the lungs outstrips the development of inflammatory phenomena in the upper respiratory tract and local lymph nodes. Twenty-four to 36 hours after infection the phenomena in the lungs predominate over the other phenomena. Beginning with this time (after 36 hours), as indicated above, secondary dissemination of the plague microbes occurs over the mucous membranes of the trachea, nose, nasopharynx, nasal sinuses because of the sputum produced by the pneumonic foci.

Based on the data obtained it may be stated that the excretion of plague microbes from a sick organism into the environment is possible throughout the entire period of the disease and that it occurs by the same route by which they penetrated into the guinea pig organism at the time of infection-- through the upper respiratory tract. However, in different periods of the pathological process this excretion differs quantitatively. In this connection the disease process can be divided into three periods.

The first period lasts up to three hours in guinea pigs. At that time, the plague microbes, after settling out on the mucosa of the upper respiratory tract after inhalation, can again be excreted from the mucous membrane into the environment. However, they are excreted in very insignificant quantities, and this can hardly be of epidemiological significance.

The second period lasts from six hours after infection to 36 hours. At this time, the plague microbes cannot be plated out from the mucous membrane of the upper respiratory tract in the majority of cases; therefore, excretion of them into the environment is not very probable.

The third period begins with 36 hours after the infection and lasts until the animal dies. It is characterized by an abundant content of plague microbes on the mucous membranes of the upper respiratory tract. As a result of this, the excretion of plague microbes into the environment together with the sputum expectorated from the patient's body may be considerable.

Therefore, the first and second periods of the disease cannot be of essential epidemiological significance, whereas the third period undoubtedly is of great epidemiological importance.

Observations made during outbreaks of pulmonary plague confirm the data which we obtained experimentally. Cases among people surrounding the plague patient have occurred, as a rule, only when the pulmonary process was fully developed in the patient. The association of healthy persons with the sick persons during the first few hours of the disease usually did not lead to infection of them (Wu-Lien-teh, 1926, 1936 and

others).

Conclusion

Based on everything presented above, we are coming to the following conclusions:

1. After inhalation infection of guinea pigs with plague the microbes not only settle on the mucous membranes of the upper respiratory tract but also penetrate into the depths of the lungs — into the alveoli, bronchioles and terminal bronchi. As early as 10 minutes after the infection plague microbes are found in different areas of the lungs, including the central portions of the pulmonary lobes.

2. Pathological changes produced by inhalation infection occur simultaneously in the upper respiratory tract and in the lungs.

3. In the lungs changes develop (clinical and morphological) which correspond to primary pneumonic plague (exudative inflammation). In the nose, trachea and large bronchi inflammatory phenomena also occur, but they have the nature of small foci and develop much more slowly than the pulmonary process.

4. Plague microbes which settle on the mucous membranes of the nose, trachea and large bronchi after inhalation are preserved here for the first three hours. During the period of time from three to 12 hours after infection the quantity of microbes decreases considerably here, and after 12 and before 36 hours no microbes are found here at all.

After 36 hours the quantity of microbes on the mucous membranes of the upper respiratory tract rapidly increases, as a result of secondary dissemination of them from pneumonic foci by sputum (possibly also as the result of hematogenous spread) and the development of acute specific inflammations in the mucosa.

5. By the inhalation method of infection peribronchial, peritracheal, mediastinal, cervical and submaxillary lymph nodes are always involved in the infectious process. However, distinct pathological changes occur in them later and develop more slowly than pneumonia.

6. A comparison of the results of investigation of the blood, lungs and other organs showed that pneumonia occurred earlier than did bacteriemia. Pneumonia was noted 24 hours after infection; bacteriemia, 36 hours.

7. Inhalation infection of guinea pigs with plague produces a primary plague pneumonia, which occurs directly as the result of entrance of plague microbes into the bronchioles and alveoli at the time of infection.

Our observations do not confirm the viewpoint of those investigators who believe that primary pneumonic plague occurs by the hematogenous route from foci originally involved in the upper respiratory tract or tonsils.

8. The results of our experiments permit us to express also the following considerations about the routes and times of excretion of plague microbes from the sick organism into the environment in

experimental primary plague pneumonia of guinea pigs: a) plague microbes are excreted into the environment through the upper respiratory tract in pulmonary plague; b) plague microbes from the mucous membrane of the upper respiratory tract can be excreted from the first few moments after infection, but excretion of them can occur on a very limited scale only which cannot be of definite epidemiological significance; c) between 12 and 36 hours after infection excretion of the microbes from the mucous membranes of the nose and trachea into the environment is not very likely; d) beginning with 36 hours after infection a secondary seeding of the mucous membrane of the upper respiratory tract occurs from the sputum produced by the pneumonic foci, because of which excretion of the microbes into the environment can occur in large quantities, which is of great epidemiological importance.

Based on all this, it may be considered that until the time that completely developed large pneumonic foci appear in the pulmonary form of plague the dissemination of microbes from the lungs in quantities adequate for aerogenic infection is not very likely.

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pp 345-347

The Problem of Treating Cases of Plague in People by Modern Drugs

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Among the modern drugs used in the treatment of plague in people are the group of sulfonamides and the antibiotic streptomycin. Practical utilization of sulfonamides for plague, as is well known, began in 1940-1941. Indian authors (S. Sokhey), noting the effectiveness of treatment with sulfonamides for bubonic plague, at the same time emphasized the advantage of this treatment in the early period of the disease. At the same time, the experience of extensive use of sulfonamides in other countries showed the inefficacy of the treatment of pneumonic forms of plague with them.

In 1945 Soviet authors (N. N. Zhukov-Vereshnikov) suggested a more effective method of treatment, recommended for all forms of plague. The method has been given the name of "comprehensive" because it uses a combination of drugs: sulfapyridine, plague antiserum, and methylene blue. At the same time, schemata were proposed for using these drugs depending on the form and severity of plague.

Before 1949, this comprehensive method of the Soviet authors was used mainly for the treatment of plague in people in China. In the practice of using this method the 24-hour doses of preparations included in the combination amounted to the following: sulfapyridine, 8-10 grams; one percent methylene blue solution, 7-10cc; plague antiserum, 40-100cc.

Experience in the treatment of 91 patients by this method in the city of Tungliao in 1949 gave the following results:

Form of Disease	Number of Persons Treated	Number Recovered	%
Bubonic	68	48	70.6
Cutaneous	1	0	0
Septic	15	1	6.6
Pneumonic	7	0	0

It should be noted that treatment of the patients was begun on the first-second day after the onset of the disease. Therefore, the treatment results using the comprehensive method were very favorable for bubonic plague. At the same time, this treatment, as is seen from the Table, did not change the usual mortality rate in the septic and pneumonic forms. The experience of treatment by the comprehensive method showed a considerable frequency of quite severe complications which depended on the preparations used. These complications occurred in the form of agranulocytosis, block of the renal tubules, overloading of the liver, etc.

Simultaneously with this group of patients and in the same city of

Tungliao another group of patients with the bubonic form of plague numbering 36 persons was treated. In the treatment of this group the comprehensive method was also used but in combination with streptomycin. The latter was given to the patient in the quantity of one gram only on the first day after his arrival at the hospital. Subsequent treatment was given by the preparations used in the comprehensive method. As the result of treatment of patients of this group 35 persons recovered and one died.

We used this method of combined treatment in 1950 in Kwangtung Province. One hundred and sixty-five patients with the bubonic form of plague were given treatment. In the treatment of this group we also continued to make certain changes. The first of them was that streptomycin began to be injected intramuscularly, whereas previously it had been administered into the bubo. Other changes referred to plague antiserum and methylene blue-- we stopped using these drugs. Simultaneously, the dose of sulfapyridine was cut in half.

The results of treatment of this group were that 161 persons recovered out of 165 patients with plague. Therefore, an undoubtedly beneficial effect was obtained with this treatment variant also.

In noting the characteristics of the clinical course of the sickness with treatment by the combined method, it should be emphasized that in the absolute majority of patients a fall of temperature to low-grade fever levels was observed 12 hours after the beginning of treatment. It returned to normal permanently after four-five days. This picture occurred under conditions of continuous treatment with sulfapyridine. The latter was given to the patients in a dose of four grams a day. With earlier stoppage of treatment the temperatures of the patients again rose, which caused us to continue sulfapyridine treatment. In these cases, recovery was delayed.

We should not overlook the fact that in patients with the bubonic form no complete resorption of the buboes was observed-- painless fibrosed structures of different sizes remained.

In the further practice of treating bubonic plague in people we, beginning with 1951, began to limit ourselves to streptomycin. Thus, for example, in 1951 all 16 patients with bubonic plague treated with streptomycin alone recovered. In the treatment with streptomycin alone the single doses of this preparation amounted to 0.25-0.5 gram; the 24-hour doses, 2-3 grams. In cases where the patient was in a serious condition the 24-hour dose of streptomycin administered was increased to 5 grams.

Everything stated above pertains to the treatment of the bubonic form of plague in people.

Proceeding with the question of treatment of pneumonic plague, it should be noted that a case with this clinical form of disease was noted for the last time in China in 1949. At that time, streptomycin was used for the treatment of six patients with pneumonic plague. All patients recovered. This experience in the treatment of pneumonic plague is small and does not permit drawing any final conclusions.

In generalizing on the results obtained from the treatment of

bubonic plague by different methods the conclusion may be drawn that at the present time streptomycin is the main drug for the treatment of plague. In various cases, it should be supplemented by sulfonamides but in a dose of no more than 4 grams a day, as has been confirmed by experience. We do not use plague antiserum or methylene blue in the practice of treating plague.

The duration of the treatment period with streptomycin naturally depends on the severity of the disease, the results of bacteriological examination, etc. On the average, treatment is limited to three-five days from the day of onset of the disease.

Aside from drugs used for treatment which may be called "specific" (streptomycin, sulfonamides), where necessary we used symptomatic agents, particularly cardiac agents (camphor oil).

During the process of treating patients with plague attention was also given to nutritional problems. It was increased and arranged in accordance with local habits and taste.

In conclusion, it should be said that the main trend in our measures for plague was its elimination. Nevertheless, we cannot stop the search for better treatment drugs for plague by means of performing experimental work on animals. This search will be continued until the final liquidation of the natural focalization of plague. In this work we count on the continuation of association and exchange of experience with Soviet plague institutions.

pp 348-355

Methods of Early Bacteriological Diagnosis of Plague

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There is no doubt at all of the fact that the earliest possible bacteriological diagnosis is of tremendous importance in every infectious disease. It is most important in plague. Accurate and rapid detection of plague infection under natural conditions is necessary for timely development of a combination of prophylactic measures. Early bacteriological diagnosis of plague in people makes it possible to save the lives of the patients by timely treatment and prevent infection of those around with plague.

We shall limit our report strictly to the presentation of materials about methods of early bacteriological diagnosis of plague. All other methods of diagnosis, not associated with isolation of plague microbe culture, will not be analysed, because they are supplementary and require obligatory final bacteriological confirmation of the existence of living plague bacteria (Bacterium pestis) in the given specific object. Only bacteriological diagnosis is of decisive importance in plague in all divisions of plague work.

Several generations of scientists have been working many years now on problems of speeding up the time of making the bacteriological diagnosis in plague. We shall mention briefly only some of the facts which have made it possible to improve substantially the methods of bacteriological investigation in this infection.

Meyer and Batchelder in 1926 suggested adding sodium sulfite to nutrient media for the purpose of stimulating growth of the plague microbe and gentian violet for suppressing the growth of putrefactive microflora. In 1931 Wright proposed using blood or its ingredients for stimulating plague microbe growth. These suggestions were firmly included in the general practice of Soviet plague institutions, thanks to the enthusiasm and persistent work of groups at the Saratov and Rostov plague institutes (Ye. I. Korobkova, G. N. Lonskaya, A. L. Berlin, V. N. Fedorov, K. S. Karpuzidi, V. M. Tumanskiy, A. P. Yashchuk, M. S. Drozhevkina, K. I. Cherkasova, Ye. E. Bakhrakh, V. V. Sakharova and many others). The next step, which was of very great importance in speeding up the time of making an accurate bacteriological diagnosis, was the use of a plague bacteriophage for maximum speed in the differential diagnosis of cultures of the plague pathogen. The plague bacteriophage was discovered, as is well known, by d'Herelle in the 1920's. In the Soviet Union plague bacteriophage was obtained for the first time in 1929 by M. P. Pokrovskaya, and then was repeatedly isolated by Yu. N. Mar'ina, A. L. Berlin and many others.

Further improvements in the method of bacteriological examination

in plague were made by the works of S. A. Vo[illegible]shchov, A. Ye. Bakulo, A. V. Sabinin and A. I. Yegorov, who in 1931 established the fact that the growth of the plague microbe is stimulated by cultures of the so-called "feeder microbes" — usually Sarcina lutea. However, only in 1950, through the investigations of K. S. Karpuzidi and L. N. Makarovskaya, did these observations culminate in the development of a concentrated dry stimulant preparation suitable for practical use and making it possible to grow plague microbes in a typical form from material containing them even in small quantities.

In our laboratory, in 1954 M. D. Pryadkina, N. N. Cutorova and G. Ya. Kivman obtained strains of saprophytic aerobic spore-bearing microbes which possessed distinctly expressed properties of stimulating the growth of plague microbes. The stimulator microbes found were studied completely and classified as B. Mesentericus fuscus and B. mesentericus vulgatus No. 66. These are long gram-positive bacilli which form spores, are aerobic, nonmotile, and possess hemolytic properties. Colonies of the stimulator microbes have the appearance of a flower: they have a dark center, rimmed by fantastic festooned brighter margins. During the course of growth on liquid media they produce stimulants, the addition of which to the nutrient media in a quantity of five percent makes it possible to grow out plague microbes from single cells.

Colonies of the plague microbe which develop on media containing these stimulants have such a typical morphology at all stages of the examination, beginning with the time of their appearance until the 17th day of growth, that recognition of them offers no difficulties. This is of very great practical importance.

A particularly important property of these stimulants is the possibility of creating optimum conditions for development and growth of plague microbes when they are added to nutrient media, even in the case of microbes which have been markedly altered under the influence of various strong and harmful environmental factors.

Thus, in the experiments of M. D. Pryadkina in obtaining new forms of plague microbes under the influence of radioactive emanations of a phosphorus isotope (P32) plague microbes were obtained the colony morphology of which had been changed beyond recognition. The first subculture of them to medium containing the stimulant substances returned their typical morphology, making it possible to determine their true plague nature.

Even more interesting are the observations of P. L. Rubinshteyn on a new stable streptomycin-dependent form of plague microbe which she obtained during the course of special experiments. Colonies of streptomycin-dependent plague microbes which could not be differentiated by the most experienced specialists grew out in a typical form which could be diagnosed without the slightest difficulty after the first subculture on medium containing five percent of this stimulator. Because of this property of "exposing" the nature of the plague microbe however it might be covered by an unrecognizable mask and however its colony morphology might be altered, we gave our preparation the name of "plague exposer"

or, in Latin, "Manifestator pestis". It has justified its distinguished name fully under whatever difficult conditions we have used it to assist us in the bacteriological diagnosis of plague.

We cannot dwell on the technique of production of Manifestator. These materials have been published. In 1956, in our laboratory, M. D. Pryadkina did work on a comparative study of different stimulators and of Manifestator pestis in experiments directed at further reduction in the time needed for making an early bacteriological diagnosis of plague in different objects, including objects very much contaminated by extraneous microflora, for example, in sputum, earth, etc.

In these experiments we used an improved preparation of Manifestator, obtained as the result of growing both producers together. For the purpose of infecting investigated objects -- sputum, earth -- plague microbes of the EV vaccine strain were used. This strain was used in model experiments in connection with the fact it belongs to the group of glycerin-negative strains, which, according to the data of M. F. Shmuter and T. V. Fedorova, grow most poorly on nutrient media. The minimum culture dose in glycerin-negative strains of the plague microbe is much greater than in glycerin-positive strains. Therefore, selective media which assure good growth of the EV strain are also selective for all other strains of the plague microbe, both virulent and avirulent.

The experiment with sputum artificially infected with the EV strain was performed in the following way: 0.1 cc of sputum containing 1,000 EV plague bacteria microbes was seeded on dishes containing Marton's agar (pH=7.3). Each of the stimulators being tested was added to it in optimum quantities. Examination of the plates under the microscope was made with objective lens No 1. Use of it makes it possible to detect the onset of growth of plague colonies much earlier than with a hand lens. It should be pointed out that in each experiment cultures were made with the same material on the same series of agar. Therefore, all the data obtained in each experiment are absolutely comparable. In this experiment the plague microbe colonies were differentiated after 19 hours of growth on medium containing Manifestator (Fig. 1a and b).

After 26 hours of growth of the colonies on medium containing Manifestator they became large; a convex center appeared in them surrounded by a definite circular zone. At the same time, on medium containing blood after 26 hours the plague microbe colonies were still very little different from the majority of colonies of common microflora contained in cultures made from sputum, and it was very difficult to differentiate them (Figs. 1, e and f).

After three days of growth of the sputum cultures the morphology of the plague microbe colonies on medium containing Manifestator continued to be typical. At this time the plague colonies were larger in their areas than the colonies of microbes of the extraneous microflora. Even a poorly experienced investigator could not help but recognize them and could not miss them.

At this time, on medium containing one-percent hemolyzed blood the morphology of the plague microbe colonies became more typical; the

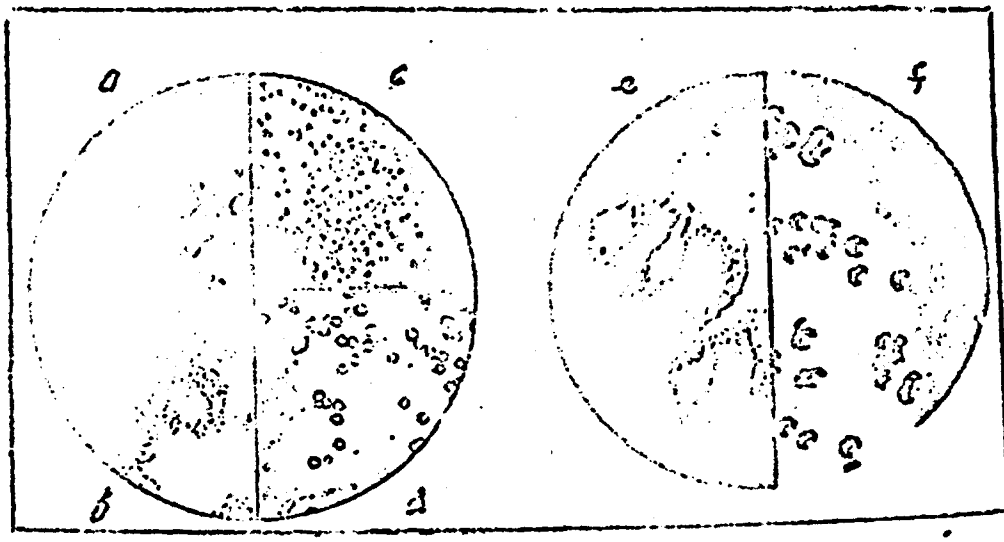

Fig. 1. Difference in Morphology of Plague Microbe Colonies Grown Out on Media to Which Five Percent Manifestator Pestis or One Percent Hemolyzed Blood Was Added (Photomicrographs from the Work of M. D. Pryadkina). a,b--plague microbe colonies after 17 and 20 hours of growth on medium containing 5% Manifestator; c,d--the same on medium containing 1% hemolyzed blood; e, plague microbe colonies after 24 hours of growth on medium containing 5% Manifestator; f, the same on medium containing 1% hemolyzed blood (in all cases a 7x ocular and a 1x objective were used).

colonies acquired a well expressed nodularity, thanks to which it became easier to differentiate them. However, their sizes were many times less than the colonies which grew out on medium containing Manifestator.

On medium containing sodium sulfite (0.025%) no growth of plague microbe colonies was obtained from infected sputum in this experiment at all (see Fig. 2 for comparison).

Therefore, in the investigation of infected sputum containing about 1,000 microbes in the culture dose on the medium containing Manifestator it was possible to make the diagnosis of plague earliest with assurance that it was correct -- after 19 hours of growth. On medium containing one percent hemolyzed blood plague colonies could be diagnosed only after 30 hours of growth, that is, 11 hours later. Such a many-hour interval in making the diagnosis of plague in infected sputum is of very great importance and makes it possible to give definite preference to media containing Manifestator over media containing blood or sodium sulfite.

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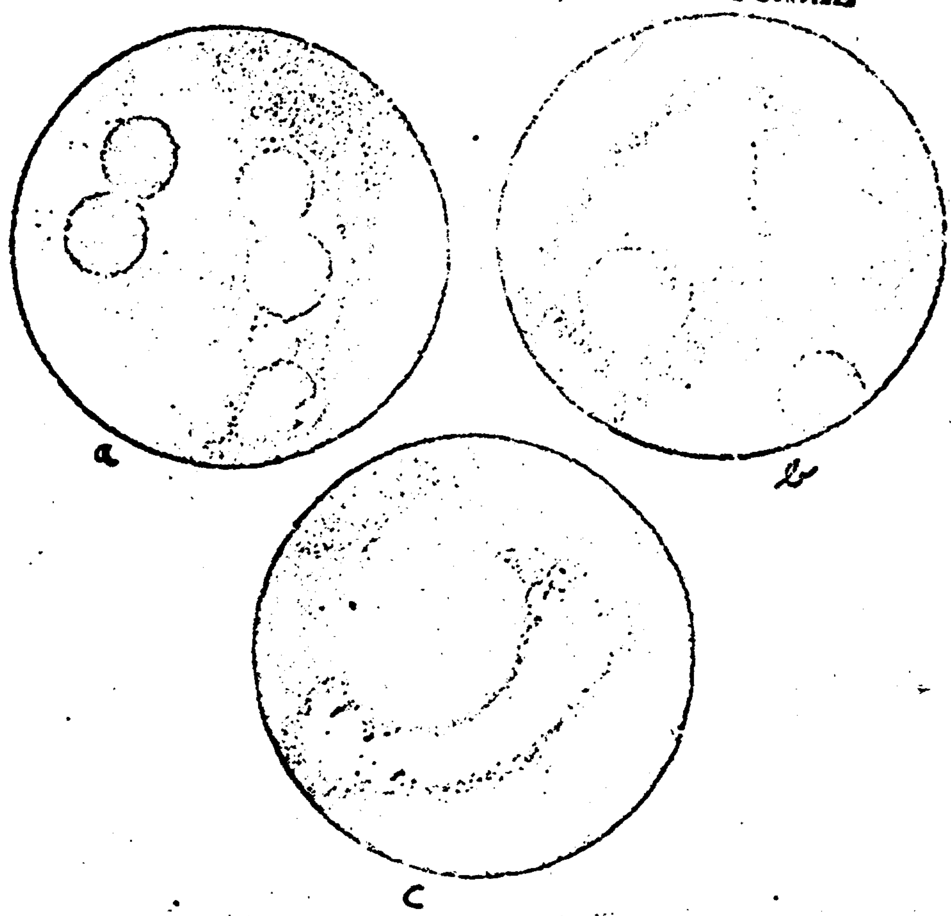

Fig. 2. Difference Between the Morphology of Plague Microbe Colonies Grown on Media to Which Different Growth Stimulants Had Been Added (Photomicrographs from the Work of M. D. Pryadkina). a. plague microbe colonies after 44 hours of growth on medium containing 1% hemolyzed blood; b. the same on medium containing 0.025% sodium sulfite; c. the same on medium containing Manifestator pestis (in all cases a 7x ocular and a 1x objective were used).

Similar experiments were performed with earth artificially infected with plague microbes of the EV strain. Just as in the experiments with sputum infected with plague microbe the plague colonies on medium containing Manifestator could be differentiated quite confidently as early as after 19 hours.

In parallel cultures containing other stimulants -- hemolyzed

[illegible] sodium sulfite — plague colonies could be diagnosed only after [illegible] hours of growth, that is, 11 hours later.

The next step in our work was the determination of the earliest time at which making the diagnosis of plague bacteriologically was possible. The first experiments were performed with material containing a considerable number of plague microbes. In this experiment the first appearance of plague microbe colonies which could be diagnosed easily was found on medium containing Manifestator after 12 hours of growth. On control medium containing blood, growth of plague colonies was also obtained after 12 hours, but they had the appearance of small round convex structures which were not only unlike those of plague but also generally resembled droplets of fluid on the agar surface rather than microbe colonies.

After 20 hours of growth the colonies on the medium containing blood were many times smaller than the colonies which grew out on medium containing five percent Manifestator pestis. After 24 hours of growth the plague colonies on medium containing Manifestator became very large with chromogenic centers and well expressed circular zones. On medium containing blood they remained small, although at this time they could be differentiated because of their rough granular surfaces.

On the basis of this experiment it may be said that with the use of material containing a large number of plague microbes the isolation of the culture and differentiation of plague colonies on media containing Manifestator is possible as early as after 12 hours of growth at 28°, whereas on medium containing blood the differentiation of plague colonies is possible only after 24 hours, that is, 12 hours later.

The situation is much more complicated with regard to the matter of making the bacteriologically diagnosis of plague in those cases where there are few plague microbes in the material being investigated and a large number of extraneous microflora. It is well known that in those cases the investigation of the material should be conducted not only by culture but also by making biological tests on laboratory or wild animals susceptible to plague. In the instructions of the Stavropol' Plague Institute made out by V. N. Ter-Vartanov, M. P. Pokrovskaya, I. G. Ioff, N. A. Miroshnichenko, N. Ye. Gubina, V. Ye. Tiflov, V. P. Babonyshev, Ye. A. Sardar, M. V. Pitsak, M. F. Shuter and others and published in 1952 it was suggested that one should not wait for the death of the biological test animal but rather use a smear from the site of infection for the bacteriological and cytological examination.

The present generation of Soviet specialists in plague mastered this method 33 years ago in Kazakhstan under the direction of senior comrades — S. M. Nikanorov and D. A. Golov, who taught them plague control and methods of bacteriological examination of smears in plague. However, science, including bacteriology, is moving steadily forward, and what satisfied us yesterday has become outdated today.

When we had such a powerful growth stimulator of plague microbes as the Manifestator pestis in our hands there were real prospects for continuing work on further shortening of the time needed for making the

bacteriological diagnosis in plague. Investigations on this problem were made by N. D. Pryadkina and N. M. Gutorova along the following lines. First of all, the time needed for taking the smears from the biological test animals was markedly reduced. Instead of 24-48 hours, which we recommended in 1952, the smears began to be taken much earlier -- one-five hours after the infection. In addition, for the purpose of further acceleration of the bacteriological diagnosis of plague guinea pigs and white mice were used as biological test animals in which the defensive reactions of the organism had been blocked. In such animals particularly favorable conditions are created for the uninterrupted multiplication of injected plague microbes, which is particulary important if there is a small number of them in the original material or if they possess a low virulence. For the purpose of blocking defensive reactions in the body use was made of an experimentally created vitamin C deficiency and the administration of cortisone.

Numerous works of Soviet and foreign investigators, particularly workers of the Stavropol' Plague Institute, A. G. Kratinov and coauthors, have shown that a vitamin C deficiency leads to a reduction in the resistance of the body to infectious diseases. The method of obtaining vitamin C deficiency in guinea pigs is very simple: over a period of 25-30 days they receive a scorbutogenic diet which consists of fodder deprived of vitamins and chiefly of vitamin C. Oats, hay, beets and bran were autoclaved for one hour at 120°.

In the weakened vitamin-deficient organism with a reduced defensive reaction of the reticulo-endothelial system the susceptibility to plague infection increases. Plague bacteria multiply in vitamin-deficient guinea pigs much more rapidly than in the bodies of normal animals.

In an experiment on the development of methods of accelerated bacteriological diagnosis of plague with the use of vitamin-deficient animals control guinea pigs were used which had received a normal diet, and guinea pigs with a marked vitamin C deficiency which had been given a scorbutogenic diet. The material for infecting the guinea pigs was sputum artificially seeded with EV plague bacteria. The infected sputum was carefully rubbed into depilated skin of the biological test animal. Smears were taken repeatedly from the infection site at different times, beginning with very early, namely after one, two, three, four, five, 12 and 24 hours. The smear obtained was seeded on Marten's agar with the addition of five percent Manifestator pestis.

As an example we are presenting an experiment on guinea pig No. 51 with marked signs of vitamin deficiency. The culture of the plague microbe was isolated at all stages of the investigation in considerably larger quantities than in the normal control guinea pig. In this experiment it was possible to isolate a pure culture of the plague microbe as early as 26 hours after beginning the examination. As a second example we should like to present an experiment on guinea pig No. 49, also with a marked vitamin deficiency. The guinea pig was infected with infected sputum. A smear was taken two hours after the infection. The culture of the plague microbe was obtained after 21 hours of growth in an incu-

tator, and the diagnosis of plague was made after 23 hours. There were many similar experiments. As a result of evaluation of them the impression is gained that multiplication of plague bacteria in guinea pigs with marked vitamin C deficiency, in which there is a disturbance in the defensive reactions of the body, occurs more actively. In such animals isolation of the plague microbe culture, even with reduced virulence, can be accomplished more rapidly and easily in a number of cases than in normal guinea pigs.

The use of media containing Manifestator contributes particularly to speeding up the bacteriological diagnosis of plague with the use of vitamin deficient test animals. This makes it possible in a short time (23-26 hours after beginning the investigation) to diagnose plague by a biological test. With the previous, even accelerated, method of investigating plague sputum the time needed for making the bacteriological diagnosis of plague through the biological test amounted to several days.

No less interesting facts were obtained in experiments where white mice were used for the biological tests in which the defensive reactions were blocked by cortisone, the suprarenal gland hormone. It has been determined by numerous investigations (K. F. Meyer, F. E. Payne, A. Larson, D. E. Walker and others) that when large doses of cortisone are administered there is a marked reduction in the resistance of the animals to different microbe organisms. The administration of cortisone suppresses the inflammatory reaction, lessens the phagocytic function of neutrophils, depresses antibody formation, weakens the digestive function of macrophages. As a result of this, after cortisone administration latent infections are activated in the organism, and the animals become susceptible even to slightly pathogenic microbes.

We used cortisone for blocking the defensive reactions in the biological test animals -- white mice -- with the aim of obtaining multiplication and generalization of slightly virulent plague microbes in them. This was done for the first time in 1955 by Meyer by intraperitoneal administration of microbes of the EV strain. We injected a culture of the EV plague microbe subcutaneously four hours after a single administration of 2.5 mg of cortisone. As early as after 24 hours in mice which received cortisone no regional lymph nodes were found. By 48 hours the weight of the spleen had decreased to 24-25 mg instead of the normal 50-65 mg. Beginning with the third day and continuing through the seventh day death of the mice occurred from plague sepsis associated with generalization of the plague infection, even after infection with vaccine strains of the plague microbes such as EV, AMP, No. 1, 17 and others.

Therefore, at the present time there is a very real opportunity of isolating strains of plague microbes even with reduced virulence by using Manifestator pestis and biological test animals in which the defensive reactions have been blocked by vitamin deficiency or cortisone. It seems to us that the methods of bacteriological investigation in plague presented make it possible to elucidate a whole series of interesting problems.

1. We can with great hope of success study the problem of the

fate of the plague microbe in the interepizootic period.

2. We can try to obtain generalization of the plague infection in camels and tarbagans after they are bitten by infected fleas.

3. It seems to us that it is possible to change the method of bacteriological examination in plague of living rodents, particularly tarbagans. Apparently, they should not be killed immediately but it is rather advisable to try to administer cortisone to them and wait for their natural deaths. If there is a latent plague infection they will possibly die after a certain period of time from plague sepsis after the defensive reactions have been blocked by cortisone. It is very interesting to study this both experimentally and under natural conditions.

4. It seems to us also that there is reason to approach the investigation of epizootic territories with the new bacteriological method, particularly in foci where plague infection is detected with difficulty. In our laboratory only the first few steps have been made in the matter of developing new principles of accelerated bacteriological diagnosis of plague. It is possible and essential to do much more.

Ivan Petrovich Pavlov said that every new forward step in a method uncovers new horizons, makes it possible to obtain new facts, to make a different approach to the solution of the problems. We should like to hope that the use and further development of the new principles in bacteriological work will make it possible to obtain new facts which will assist in the solution of interesting and very important problems of epizootology and epidemiology of plague.

As a result of investigations made the following may be stated: 1. The use of the "Manifestator pestis" preparation makes it possible to accelerate considerably making the bacteriological diagnosis of plague.

2. When there is a large number of plague microbes in the original material bacteriological diagnosis can be made as early as after 12 hours, that is 12-14 hours earlier than on media containing hemolyzed blood.

3. When no more than 1,000 plague cells are contained in the culture dose along with the extraneous microflora in a culture of sputum, earth, etc. the bacteriological diagnosis of plague may be made with the use of Manifestator after 19 hours, that is, 11-13 hours earlier than on medium containing blood.

4. The use of biological test animals for investigating material contaminated with extraneous microflora (sputum, earth, dead bodies which are beginning to decay, etc.), the use of Manifestator and early aspirates from the infection site in normal and particularly vitamin-deficient animals permits the bacteriological diagnosis of plague as early as 23-26 hours after beginning the examination.

5. The use of cortisone for blocking the defensive reactions in white mice (when they are used as biological test animals) makes it possible successfully to isolate plague bacteria with reduced virulence and pathogenic properties.

6. Large-scale plant production of the Manifestator pestis preparation should be organized for the needs of the plague organization.

pp 336-350

Side-Effects Produced by Living "1,17" Plague Vaccine

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In the prophylaxis of plague in man, a great part is played by vaccination. Prior to 1954 avirulent living vaccine was used in the Soviet Union, made from the EV strain of Robic and Girard. In recent years, through the works of a group of scientific workers of the State Scientific Research Institute of Microbiology and Epidemiology of South-east USSR ("Mikrob") and other plague institutes the advisability of changing to another, more immunogenic vaccine was substantiated for immunization of people; this vaccine was given the name "dry living 1,17 plague vaccine", which is used at the present time for plague prophylaxis in the Soviet Union. According to instructions vaccination may be given subcutaneously, intradermally and percutaneously, whereby preference is given to the intradermal method as assuring a stronger immunity in those vaccinated.

During the course of vaccination by the intradermal method in practice medical workers came up against increased reactivity of persons inoculated by this method. In various cases, at the injection site of the vaccine areas of necrosis and sterile abscesses occurred, and not uncommonly vaccination was accompanied by a temporary loss of the ability to work. Considering the mass complaints of the population of the side effects produced by the vaccine when it was given intradermally, we made observations of various groups of people vaccinated by different methods. The aim of this observation was a study of the side effects of live dry plague "1,17" vaccine by comparison with EV vaccine in different methods of administration of them (intradermally, subcutaneously and percutaneously).

Organized population groups, mainly worker's brigades occupied in control of rodents and workers in plague institutions, were vaccinated.

For each method of vaccination an individual group was selected. Those to be inoculated were first given a medical check-up, and afterwards they were observed. On the first day after the vaccination, check-ups were made after six, 12, 18 and 24 hours; subsequently, twice a day, that is, morning and evening, until the reaction to the vaccine disappeared. Consideration was given to the temperature, the person's feeling of well-being, the local skin reaction and the reaction of the regional lymph nodes. The data obtained are summarized in Table I.

Acquaintance with Table I permits us to draw the conclusion that with the use of "1,17" vaccine the percutaneous method of vaccination produced the least side effects; with it there was no marked general reaction or severe local signs or loss of the ability to work.

Depending on the method of inoculation, the local reaction varied

Table I

Comparative Data on the Side Effects Produced by Vaccination against Plague with Different Vaccination Methods, using "1,17" and EV Strains

Показатели	Вакцина «1,17» внутрикожный: первая прививка	Вакцина «1,17» внутрикожный: повторно через 1 год	Вакцина «1,17» накожный	Вакцина «1,17» подкожный	Вакцина ЕВ накожный	Вакцина ЕВ подкожный
Количество вакцинированных	230	22	176	75	915	697
% из них, у которых отмечены:						
Инфильтрат и покраснение на месте введения размером:						
1,1×5,0 см	12,1	9,1	0	2,7	0	76,2
5,1×10,0 »	35,6	27,3	0	97,3	0	12,1
10,1×15,0 »	46,5	59,1	0	0	0	0,9
15,1×20,0 »	5,6	4,5	0	0	0	0
Болезненность места введения	96,1	100	0	100	0	89,1
Стерильные абсцессы на месте введения	0,8	0	0	0	0	0
Реакция регионарных лимфатических узлов	17,4	13,2	2,8	93,.	0	12,2
Лимфангоит	12,1	13,6	0	0	0	0
Повышение температуры до:						
37,0–38,0°	59,5	54,5	6,8	93,3	2,3	13,9
38,1–39,0°	12,2	18,2	0	20,0	0,3	3,3
39,1–40,0°	0,8	0	0	0	0	0,1
Продолжительность лихорадочного периода						
1 день	19,5	22,7	3,8	16,0	1,8	9,8
2 дня	25,6	31,8	0	64,7	0,4	3,3
3 »	10,4	13,6	0	14,6	0	0,9
4 »	3,0	4,5	0	0	0	0
7 дней	0,4	0	0	0	0	0
10 »	0,4	0	0	0	0	0
Головные боли	52,6	59,1	4,5	44,0	4,1	64,8
Озноб	44,3	54,5	1,7	28,0	1,0	41,6
Общая слабость (недомогание)	58,3	63,6	7,4	62,6	2,6	62,9
Тошнота	10,4	22,7	0	9,3	0,2	3,1
Рвота	1,7	0	0	2,7	0	1,3
% лиц, потерявших трудоспособность на:						
1 день	3,5	4,5	0	1,3	0,2	4,0
2 дня	9,6	9,1	0	10,6	0,1	1,9
3 »	0,4	0	0	1,3	0	0,3
4 »	0	0	0	0	0	0
13 дней	0,4	0	0	0	0	0
16 »	0,4	0	0	0	0	0

Note: 1. in those vaccinated intradermally with "1,17" vaccine the infiltrate, erythema and pain at the injection site were absent; only

[continued next page]

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edema and erythema were noted along the course of the "scratches", and in various cases there was a vesicular eruption and slight pain. 2. in those vaccinated percutaneously with EV vaccine only edema and erythema were noted along the course of the scratches and slight pain. 3. the percentage of persons with elevated temperature is given as a cumulative sum, that is, those persons in whom the temperature reached 39.1-40.0° are included in the previous groups (38.1-39.0° and 37.0-38.0°). 1. indices; 2. "1,17" vaccine; 3. intradermal; 4. first inoculation; 5. a second time after one year; 6. percutaneous; 7. subcutaneous; 8. EV vaccine; 9. percutaneous; 10. number of vaccinees; 11. % of them in whom the following were noted: 12. infiltrate and erythema at the injection site measuring: 13. pain at the injection site; 14. sterile abscesses at the injection site; 15. reaction of the regional lymph nodes; 16. lymphangitis; 17. temperature elevation to: 18. duration of febrile period; 19. day (s); 20. headaches; 21. chill; 22. general weakness (malaise); 23. nausea; 24. vomiting; 25. % of persons who were unable to work for:

quite considerably. In the case of subcutaneous inoculations with "1,17" vaccine, erythema and infiltrates up to 5x10 centimeters in area were noted at the injection site in almost all persons vaccinated. In the case of intradermal inoculations, in the great majority of those inoculated erythema and an infiltrate occupied an area of 5x10-10x15 centimeters (in 189 out of 230 persons inoculated) and after intradermal and subcutaneous vaccinations they were accompanied by considerable pain. The greater the area of erythema and infiltrate the more marked was the pain and vice versa. About one third of the inoculees had to hold their arms semiflexed at the elbow joint for two or three days after the vaccination, not being able to use them. In the case of percutaneous inoculations, only erythema, slight edema and, in various cases, a fine vesicular eruption along the courses of the scratches on the skin appeared at the injection site of the "1,17" vaccine.

The basic manifestation of the general reaction was fever, which usually appeared on the day of the inoculation. In the case of percutaneous vaccination with "1,17" vaccine the temperature elevation was observed in isolated cases, did not exceed 38°, and lasted no more than a day. In the case of subcutaneous inoculations the fever was observed in almost all vaccinated persons, whereby in 15 out of 75 persons (20 percent) the temperature was higher than 38°. The duration of fever by this method of vaccination was equal to one or two days in the majority of cases. However, in various cases the temperature elevation lasted up to three days. In a somewhat smaller percentage of cases than after subcutaneous vaccination fever was observed in persons vaccinated intradermally (in 137 out of 230 cases, 59.5 percent).

The reaction in the regional lymph nodes was observed in almost all those vaccinated subcutaneously, to a considerably lesser degree in those vaccinated intradermally, and only from time to time in those

vaccinated percutaneously. This reaction in various cases was expressed as an enlargement of the glands to the size of a large pea and in pain. Lymphangitis was observed only in persons vaccinated by the intradermal method (in 28 out of 230 persons vaccinated, or 12.1 per cent of the cases). The reaction of the regional lymph nodes developed in persons vaccinated during the first day after the inoculation and disappeared simultaneously with the disappearance of the local skin reaction. In two cases in those vaccinated with "1,17" vaccine intradermally we observed the occurrence of sterile abscesses which were accompanied by a marked local reaction and loss of the ability to work for 13-16 days.

There were no losses of the ability to work in those vaccinated percutaneously. At the same time, in those vaccinated by the intradermal method it was noted in 14.3 per cent of the cases; in those vaccinated subcutaneously, 13.2 per cent of the cases, and lasted from one to three days.

The commission which studied and approved the bivalent living dry plague vaccine "1,17" (Altareva, Antonov, Zhdanov, Korobkova, Kotlyarova, Lenskaya, Lobanov, Mikhaylova, Pastukhov, Savostin, Tumanskiy, Yashchuk 1957) notes that the side effects from this vaccine are greater when it is used intradermally than after percutaneous use both with respect to the number of mild and moderately severe general reactions to the inoculation, and the total number of reactions developing.

Ye. I. Korobkova (1956) points out that the intradermal method of vaccination suggested by D. G. Savostin gives the greatest effect in the protection against plague under experimental conditions. An important factor in the intradermal inoculations is the possibility of accurately dosaging the quantity of vaccine injected. At the same time, Ye. I. Korobkova emphasizes that the negative aspects of the intradermal inoculations are the technical difficulties in carrying them out and the increased local reaction to the inoculation (formation of a pustule). The percutaneous method of inoculating the living vaccine, Ye. I. Korobkova writes, deserves special attention because of its lack of side effects, its adequate immunological effectiveness, judging by experiments on animals, as well as its simplicity and ease of giving the inoculations in practice.

Having at our disposal data on the side effects of EV plague vaccine, we considered it necessary to present them in Table I for comparison with the side effects of living dry "1,17" plague vaccine. There were 697 persons under observation who had been vaccinated with EV vaccine subcutaneously and 915 persons vaccinated with it percutaneously. The method of recording the reactivity in these persons was the same as in those vaccinated with the "1,17" vaccine.

On the basis of the materials presented in Table I, it may be concluded that EV vaccine produced fewer side effects than "1,17" vaccine. This applied both to the local and general reactions in vaccinated persons. At the same time, in those inoculated with the EV vaccine the local and general reactions were much less pronounced when the vaccine was applied percutaneously than after injection by the subcutaneous method.

G. G. Nepryakhin, Ye. I. Novikova, Ye. P. Gur'yeva (1955) also reported a low febrile reaction and a local reaction from subcutaneous inoculations of EV vaccine. In order to evaluate the side effects of the vaccine at the time of a second vaccination, part of the persons (22 persons) inoculated with "1,17" vaccine intradermally was vaccinated a second time with the same vaccine and by the same method a year after the first vaccination. From Table I it is seen that there was no increased reactivity in those who were revaccinated.

Everything presented above constitutes evidence to the effect that the inoculation method producing fewest side effects after vaccination with living dry "1,17" plague vaccine is the percutaneous method. The other two methods of injecting the vaccine, recommended by the instructions, are so productive of side effects that one involuntarily wonders whether it is advisable to use them.

Pronounced local and general reactions, the occurrence of sterile abscesses in various cases, the loss of the ability to work have given us the idea that inoculations against plague should be given by the percutaneous method. If the indubitable advantage of the intradermal method of vaccination over the percutaneous method is definitively proved, extensive use of the intradermal method of vaccination may be permitted only when there is adequate epidemiological basis for it.

Conclusions

1. Intradermal and subcutaneous inoculations against plague with "1,17" vaccine are associated with a considerable general and local reaction in those vaccinated and produce loss of the ability to work for one to three days. In two out of 230 cases sterile abscesses occurred as the result of the intradermal inoculation. At the same time, the percutaneous method of inoculation is characterized by the least general and local reactions, and for this reason it should be recommended as the basic method for giving mass vaccinations.

2. The intradermal method should be recommended in cases of emergency vaccination when antiepidemic measures are being taken in an area of a plague focus, in places where plague epizootics have been noted among small mouse-like rodents and in workers of plague institutions working with virulent strains of plague microbes.

3. In comparing the side effects of living plague "1,17" vaccine with EV vaccine, EV vaccine was found to be less productive of side effects after subcutaneous injection. With the percutaneous method no essential difference was noted between the vaccines with regard to the production of side effects.

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pp 361-366

Side Effects Produced by "1,17" Plague Vaccine Depending on its Cellular Composition after Intradermal and Percutaneous Injections

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Study of the side effects produced by bivalent "1,17" plague vaccine was made in February-March 1956. (The work was done with the participation of the following physicians of the plague departments: T. A Verivodina, T. P. Kudinova, N. V. Bryantsova and V. L. Shatalova). In all, five series of vaccine were tested released by the Central Asiatic Plague Institute, the characteristics of which at the time of their release and at the time of inoculation are presented in Table I.

Table I

Characteristics of Series of "1,17" Vaccine Investigated for Side Effects

№ серии	При выпуске вакцины				При применении вакцины			Выросло колоний	
	число доз в ампуле	концентрация по оптич. стандарту (в млрд.)	% живых клеток	остаточная влажность (в %)	концентрация по оптич. стандарту (в млрд.)	число микробных тел в одной дозе (в млрд.)	% живых клеток	глицерино-положительных	глицерино-отрицательных
146/1	20	40	11,0	4,46	25,0	5,2	2,0	4	0
146/2	49	40	28,0	3,56	10.0	2,0	1,0—2,0	1	0
152/1	60	45	34,0	4,84	8,6	1.7	6.9	7	3
162/2	63	40	52,0	4,40	7,5	1,5	41,3	62	1
165/1	43	36	31,0	4,60	7,5	1,5	30,0	38	4

Notes: 1. longevity of the vaccines-- May-June 1956; 2. the interrelationship of the cells of the glycerin-positive and glycerin-negative variants was determined by means of culture on two plates containing 100 microbes each (according to the optical standard) and individual checking of all the colonies which grew out on Kolya Bol'kur's medium and on liquid medium containing 1% glycerin and an indicator. 1. number of series; 2. at the time vaccine was released; 3. number of doses in the ampoule; 4. concentration according to the optical standard (in billions); 5. % of living cells; 6. residual moisture (in %); 7. at the time the vaccine was used; 8. number of microbes in a single dose (in billions); 9. colonies which grew out; 10. glycerin-positive; 11. glycerin-negative.

From the data included in Table I it is seen that the series of vaccine tested were not standard. At the time of utilization in some cases, the percentage of living cells was considerably reduced (to

one-two per cent in series 146/1 and 146/2). In all series of vaccine cells of the glycerin-positive variant of plague microbe predominated (number 17).

Consideration of the side effects of the vaccine was made in 1,658 persons; of these 968 were inoculated intradermally and 690 percutaneously (see Table II).

Table II

Number of People Vaccinated by Different Methods and Series of Vaccine

Серия вакцины (1)	(2) Вакцинировано		
	внутрикожно (3)	накожно (4)	всего (5)
146/1	98	17	115
146/2	198	176	374
152/1	246	45	291
162/2	177	325	502
165/1	249	127	376
Всего: (5)	968	690	1568

1. series of vaccine; 2. vaccinated; 3. intradermally; 4. percutaneously; 5. total.

Observations of the reactions of all those vaccinated were made by physicians beginning with 12 hours after the inoculations and up to 72 hours. Thereby, the following indices were noted: 1) the size and time of appearance of the reaction at the injection site of the vaccine (erythema and an infiltrate, the formation of vesicles and pustules, the duration of preservation of these indices); 2) the reaction of the lymph nodes and lymphatics (lymphangitis, pain in the area of the lymph nodes, enlargement of the lymph nodes and the duration of preservation of these signs); 3) general manifestations of the reaction to the vaccine (headache and its duration, temperature elevation and the duration of the elevated temperature, general malaise, the presence of gastrointestinal disorders in the form of nausea, vomiting, diarrhea, loss of the ability to work for several days).

Side Effects Produced by the Vaccine in Those Inoculated Intradermally

The local reaction after intradermal inoculations was expressed in the form of erythema and an infiltrate, the appearance of pustules, lymphangitis, pain in the area of the lymph nodes. The erythema and infiltrate were noted in all 968 persons vaccinated. In 957 of them the sizes of the areas of erythema and the infiltrate were measured, and these

were found to occupy an area of less than 25 square centimeters in 365 or 38.8 per cent; from 25 to 50 square centimeters in 203 persons (21.2 per cent); 50 to 100 square centimeters or more in 389 persons (40.6 per cent). The duration of the areas of erythema and the infiltrate, as recorded in 950 persons inoculated amounted to the following: less than 24 hours, 203 persons (21.3 per cent); from 24 to 48 hours, 362 (37.9 per cent); and from 48 to 72 hours in 390 persons inoculated (40.8 per cent).

Pustules were noted in 455 persons (47 per cent), whereby they were maintained up to 24 hours in two inoculees (0.2 per cent); from 24 to 48 hours in 141 (14.6 per cent) and more than 48 hours in 312 inoculees (32.2 per cent).

An inflammatory reaction of the lymphatics (lymphangitis or pain in the area of the lymph nodes) was found in 435 inoculees (44.9 per cent). Its duration was the following: less than 24 hours, in 77 (8.0 per cent); 24 to 48 hours, 224 (23.1 per cent); more than 48 hours, 134 inoculees (13.8 per cent).

Enlargement of the regional lymph nodes was noted in 203 persons (21 per cent); of these the nodes reached the size of a pea in 86 (8.9 per cent); the size of a kidney bean, in 85 (8.8 per cent); and the size of a plum or larger, in 32 (3.3 per cent).

The general manifestations of the reaction to the vaccine at the time of its intradermal injection were expressed as malaise, headache, temperature elevation, signs of a gastrointestinal disorder and loss of the ability to work.

Malaise was noted in 448 persons (46.3 per cent); headache, in 564 (58.3 per cent), whereby it lasted for 24 hours in 141 inoculees (14.6 per cent); from 24 to 48 hours, in 341 (35.2 per cent); and more than 48 hours, in 82 inoculees (8.5 per cent).

A temperature elevation was found in 390 inoculees (40.3 per cent); of these it rose to 37.5° in 140 persons (14.5 per cent); 37.5 to 38° in 179 (18.5 per cent); and from 38° to 39° , in 71 (7.3 per cent). Elevated temperature remained for 16-24 hours in 25 inoculees (2.6 per cent); 24 to 36 hours in 281 (29.0 per cent); and 36 to 48 hours in 84 (8.7 per cent).

Gastrointestinal disorders were found in 112 persons (11.6 per cent).

In part of those vaccinated loss of the ability to work was noted for one-three days. In all, loss of the ability to work was found in 163 persons (17.4 per cent) with a total loss of 212 workdays. One hundred and thirty one persons lost the ability to work for one day (13.6 per cent); 30 (3.1 per cent), for two days; seven (0.7 per cent), for three days.

On the basis of the data presented we have derived in a general form the indices for the local and general reactions to intradermal injection of plague "1,17" vaccine. In determining the intensity of the reaction we adhered to the instructions of the "Mikrob" Institute. A general evaluation of the nature of the reaction to intradermal injection

of the vaccine is given in Table III.

Table III

The Nature of the Reaction to Intradermal Injection of Vaccine in 968 Inoculees

1 Характер показателей	2 Всего реагиро-вали	3 Характер реакции		
		4 Слабая	5 Средняя	6 Сильная
		7 Общая реакция		
9 Абсолютные цифры . .	665	271	272	112
10 Проценты	67,7	28,0	28,1	11,6
		8 Местная реакция		
9 Абсолютные цифры . .	968	155	371	438
10 Проценты	100	16,1	38,5	45,4

Note: The local reaction occurred in all 968 persons inoculated, but its degree was noted in only 964 inoculees. The percentages in the last line of the table were calculated with respect to this number. 1. nature of the indices; 2. total reacted; 3. nature of reaction; 4. weak; 5. moderate; 6. strong; 7. general reaction; 8. local reaction; 9. absolute figures; 10. percentages.

From the data presented in this table, it is seen that the intradermal injection of plague "1,17" vaccine very frequently produces a striking general and local reaction in the inoculees and a reaction in the regional lymph nodes.

Side Effects Produced in Those Inoculated Percutaneously

In contrast to those vaccinated intradermally, the reaction to percutaneous vaccination was slight in the inoculees. Erythema and an infiltrate were noted in 266 persons (38.6 per cent), whereby in all cases they were slight, chiefly along the courses of the scratches. Of these 266 persons the local reaction (slight erythema and an infiltrate) was observed less than 48 hours in 96 (13.9 per cent) and less than 24 hours, in 170 (24.7 per cent). Vesicles and pustules were noted in eight persons (1.2 per cent). Persons with enlargement of the lymph nodes were not found, and pain in the area of the lymph nodes was noted in only two persons.

Of the general manifestations the following were noted: headache in 12 inoculees (1.7 per cent); malaise, in four (0.6 per cent); signs of a gastrointestinal disorder, in one; and loss of the ability to work for

one day, in one inoculum.

Therefore, in contrast with those vaccinated intradermally, practically no general reactions were observed in those vaccinated percutaneously with the exception of a slight infiltrate and erythema along the scratches in the skin. Other, slight reactive manifestations were noted only in individual persons.

Reasons for the High Degree of Side Effects Produced by "1,17" Vaccine on Intradermal Injection

Elucidation of the problem of what the high degree of side effects of the "1,17" plague vaccine is associated with after intradermal injection of it is very interesting: whether it is a reaction to the toxin of the plague microbes, or associated with survival of the microbes at the injection site, or, finally, with the interrelationship of the glycerin-positive (number 17) and glycerin-negative (number 1) strains in the vaccine. The answer to these questions is of importance for proper production of the vaccine.

One of the authors (Shmuter) in cooperation with F. M. Chulturova made experiments on guinea pigs in 1955 for clarifying the part played by individual components of the vaccine as well as the percentage of living microbes in the vaccine in the side effects produced by the latter. As a result of these experiments, the following was established: 1. the local and febrile reactions after injection of vaccine depend on the percentage of living cells in the vaccine. The injection of killed vaccine is associated with a slight temperature reaction and a slight reaction at the injection site; when guinea pigs were injected intradermally with vaccine containing a high percentage of living cells a considerable temperature rise was noted and a distinct reaction at the injection site.

2. The general reaction, as read by the data on change of weight, as well as the reaction in the regional lymph nodes did not depend on the percentage of living cells in the vaccine.

3. The reaction to injection of the vaccine prepared from strain number 1 in the guinea pigs was more pronounced than that to the injection of vaccine prepared from strain number 17.

For the purpose of elucidating the significance of the factors in the different side effects produced by individual series of vaccine, we compared the nature of the reactions in persons vaccinated by two different series of vaccine containing different percentages of living cells at the time of application of the vaccine in Table IV; therefore, we compared different numbers of microbes in the vaccine dose.

We did not succeed in determining any relationship between the side effects produced by the vaccine and the interrelationship of strains 1 and 17 in it, because in all of the vaccines series used for study there was a marked predominance of the percentage of living glycerin-positive cells, that is, of strain 17, and only in vaccine series 152 were the living cells of the glycerin-negative variant relatively more (see Table 1). It should be noted that the injection of the vaccine series 152 was

Table IV

The Relationship Between the Side Effects Produced by Vaccines of Different Series and Different Percentages of Living Cells (Series 146/1-Two Per Cent Living Cells, 5.2 Billion Microbes in the Vaccine Dose; Series 165/1, 30 Per Cent Living Cells, 1.5 Billion Microbes in the Vaccine Dose)

1 Характер реакции	2 % привитых с данной реакцией от вакцины:	
	146/1	165/1
3 Покраснение и инфильтрат площадью более 50 см²	77,8	86,3
4 Сохранение покраснения и инфильтрата более 48 часов	48,3	87,2
5 Наличие везикул и пустул	32,6	61,4
6 Лимфангоит и болезненность в области подмышечных лимфатических узлов	42,9	23,9
7 Увеличение регионарных лимфатических узлов	23,4	39,1
8 Головная боль	36,7	71,3
9 Сохранение головной боли более 24 часов	10,2	49,0
10 Повышение температуры	17,4	38,5
11 Температура выше 37°	12,2	37,3
38°	9,2	29,8
12 Общее недомогание	35,7	67,5
13 Кишечные явления	5,1	18,1
14 Потеря трудоспособности	4,1	16,9

1. nature of reaction; 2. % of inoculees with the given reaction from vaccine: 3. erythema and infiltrate of an area of more than 50 square centimeters; 4. erythema and infiltrate from more than 48 hours; 5. the presence of vesicles and pustules; 6. lymphangitis and pain in the area of the axillary lymph nodes; 7. enlargement of the regional lymph nodes; 8. headache; 9. maintenance of headache more than 24 hours; 10. temperature elevations; 11. temperature higher than 37°; 12. general malaise; 13. intestinal phenomena; 14. loss of the ability to work.

accompanied by a more pronounced reaction than injection of the vaccines of the other series.

Data presented in Table IV are evidence to the effect that injection of vaccine of series 165/1 with a high content of living cells (30 per cent) was accompanied by a more active and more prolonged reaction by comparison with what was produced by vaccine 146/1 with a low content of living cells (two per cent). The latter is in agreement with data obtained in experiments on the vaccination of guinea pigs.

It should also be pointed out that in a number of cases a considerable difference was noted in the reactions of persons vaccinated with the same series of vaccine but taken from different ampoules. This was apparently associated with the fact that the ~~vaccine of one series~~

contains different number of living cells in different ampoules frequen-ly and differs in the interrelationship of glycerin-positive and glycer-in-negative variants included in the vaccine. We noted the latter dif-ference in control cultures of the vaccine.

Conclusions

1. The intradermal inoculation of "1,17" plague vaccine was us-ually accompanied by a striking general and local reaction and reaction of the lymphatics of the regional lymph nodes.

2. The local reactions were noted in all the inoculees, and they were of moderate severity in 38.5 per cent; severe, in 45.4 per cent. The reaction was expressed in the appearance of an infiltrate and ery-thema, which in 40.6 per cent of the cases reached 50 to 100 or more square centimeters. In almost half of those vaccinated the formation of vesicles and pustules was noted, whereby in the majority the pustules re-mained for two or three days.

3. The reaction of the regional lymphatic system was expressed as inflammation of lymphatics and pain in the area of the axillary lymph nodes in 44.9 per cent of the inoculees and enlargement of the lymph nodes in 21.0 per cent.

4. A general reaction was noted in 67.7 per cent of the inoculees of them, it was of moderate severity in 28.6 per cent; severe, in 11.6 per cent. It was expressed as malaise (46.3 per cent of those inocula-ted), headache for one-three days (58.3 per cent), temperature elevation (40.3 per cent, whereby it was over 38° in 7.3 per cent), gastrointes-tinal disorders (11.6 per cent) and loss of the ability to work for one-three days (17.4 per cent).

5. Percutaneous vaccination with plague "1,17" vaccine practically produced neither local nor general reaction. Usually, only erythema and a slight infiltrate were noted along the course of the scratches.

6. The nature of the reactive manifestations in inoculees, the in-tensity and particularly the duration of them were to a considerable de-gree connected with the percentage of living cells in the vaccine. The injection of vaccine with a high percentage of living cells is accompan-ied by a more pronounced reaction.

7. In a number of cases, when the vaccine is used three months after its preparation a very small percentage of living cells is present in it, and the number of cells of the glycerin-negative variant is negl-gible in the majority of series. The difference in the number of living cells was noted not only between different series of vaccine but in a number of cases also in ampoules of the same series.

8. Considering the great degree of side effects produced by the intradermal method of injecting the plague "1,17" vaccine, the use of this method may be recommended only if there are special indications.

9. It is necessary to obtain a vaccine with more stable proper-ties both with respect to the percentage of living cells in it and with respect to the interrelationship of glycerin-negative and glycerin-positive variants.

6934

pp 367-371

The Problem of Optimum Dosage of Dry Living "1, 17" Plague Vaccine.

Report 2. The Effectiveness and the Side-Effect Production of the Vaccine in Accordance with the Vaccinating Dose and Methods of Vaccination.

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In our previous work (N. R. Ivanov and V. K. Klochkova. The Problem of Optimum Dosage of Dry Living Plague Vaccine. Report 1. Works of the "Mikrob" Institute, No 2, Saratov, 1958), in experiments on guinea pigs and in the vaccination of human volunteers we established the optimum vaccinating dose for bivalent dry living "1, 17" plague vaccine containing 10 percent living cells (10 percent survival). In subsequent investigations we made an attempt to clarify the effectiveness and side-effect production of this vaccine in accordance with the percentage of living cells in it, the size of the dose being used for vaccination and the method of vaccination.

In accordance with instructions on the preparation and application of bivalent dry living plague vaccine one (single) dose for intradermal and subcutaneous methods of vaccination should be equal to 1,500,000,000 microbes if the survival rate of the vaccine amounts to 20 percent or higher. With a survival of vaccine of less than 20 percent it is necessary correspondingly to increase the total number of microbes in the dose. For example, if the survival rate of the vaccine is 10 percent its single dose should contain 3,000,000,000 microbes. Therefore, the dose used can contain either 1,500,000,000 or 3,000,000,000 microbes. The number of living microbes included in one dose can be equal to 300,000,000 or may come close to 1,000,000,000-1,500,000,000 if the survival rate of the vaccine comes close to 80-100 percent. Therefore, in the case of vaccination with living dry plague vaccine the standard dose, essentially, is not used. In determining the single dose of the vaccine, the principle of calculation either by the number of living microbes or by the total number of microbes in the dose does not stand up.

Experience in the use of bivalent vaccine on people showed that different series of it possess different

degrees of side-effect production. Production of side-effects may depend on three factors: 1) on the fact that the dose used for vaccination is too high; 2) on the presence of a large number of dead microbes in the dose; 3) on the presence of a large number of living microbes in the dose. Each of these factors is decisive, accounting for the side-effect production of the vaccine, and the effectiveness of the vaccine is not known exactly, because the problem of comparative effectiveness of vaccination in accordance with the absolute size of the dose used and the number of living microbes in it has not been adequately studied.

For the purpose of solving this problem an experiment was performed on 490 guinea pigs. The animals were vaccinated with three series of dry living bivalent vaccine with different survival rates (11, 4, 30, 9 and 47.9 percent) as well as with a suspension of fresh two-day culture of bivalent vaccine in which the percentage of living microbes was considered close to 100. For each dry vaccine a study was made of three doses--10,000, 10,000,000, 1,000,000,000 living microbes whereby the dose of vaccine was not determined by the total number of microbes but rather by the number of living microbes. With the same number of living microbes in the dose the total number of microbes being injected differed, which made it possible for us to determine the effect of living and dead microbes on the effectiveness and side-effect production of the vaccine.

With the aim of determining the effectiveness of the vaccination method guinea pigs were vaccinated by three generally accepted methods, that is, subcutaneously, intradermally and percutaneously accoring to the modification which we have suggested (see below).

As has been shown by experimental investigations of D.G. Savostin, G. N. Lenskaya, Ye. I. Korobkova and other authors, the most effective methods of vaccination are interdermal and percutaneous. However, in the case of interdermal vaccination with bivalent vaccine stormy local and general reactions to the inoculation were noted in experimental animals and people.

In attempting to preserve the effectiveness of the interdermal method of vaccination and, at the same time, reduce the local and general reactions to the inoculation, one of us (Ivanov) suggested a modification of the intradermal method of vaccination in which the natural route of infection with plague (the bite of fleas) was simulated. For this purpose we used a special instrument, which consists of a metal cylinder six centimeters in length, in which there is a movable plunger with ordinary sewing needles mounted on its base projecting two millimeters above the base of the plunger. The

technique of vaccination with this instrument is simple. The inoculation site on the volar surface of the forearm is treated. The vaccine is applied in three places (as in the case of percutaneous vaccination), after which, the instrument is applied to those places, the plunger is raised, and the needle is injected into the skin in a manner similar to a puncture with Francke's spring lancet. The vaccine enters the skin intradermally, and the vaccine process develops. In the case of vaccination by the percutaneous method and the intradermal method in our modification the dose of vaccine (as in the case of vaccination of people) was made 10 times larger than after intradermal and subcutaneous vaccination.

The vaccinated animals were infected subcutaneously 21 days after vaccination with 200,000 CLD (10,000,000 microbes) of a virulent strain of the plague microbe (No 708).

In vaccinated animals before infection and after it a study was made of hematological changes, the opsono-phagocytic reaction, the local and the general reaction to the inoculation. In the present report material has been presented only on the survival rate of animals after infection and the degree of expression of the local and general reactions to the inoculation.

As is seen from Table 1 and Fig. 1, with increase in the number of living microbes in the dose the percentage of animals surviving after the infection increases with all methods of vaccination. Thereby, it should be emphasized that vaccines with a high survival rate protect a higher percentage of animals against death than do vaccines with a low survival rate (see Table 1).

In our experiment the total number of microbes injected into the animal organism at the time of vaccination decreases with increase in the percentage of living cells in the vaccine. From Fig. 2 it is seen that the strength of post-vaccinal immunity depends specifically on the number of living microbes in the dose rather than on the total number of microbes injected.

The degree of expression of the local and general reactions to the inoculation was different depending on the percentage of living microbes in the vaccine. With the same dose of vaccine more vigorous local and general reactions were observed to the inoculation when vaccines with low (11.7) and very high (100) survival rates were used. Therefore, increase in the number of dead microbes in the vaccine reduces the effectiveness, thereby increasing side-effect production. At the same time, a marked increase in the number of living microbes in the vaccine (close to 100 percent) also increases its side-effect production, which, however, is accompanied by an increase in the effectiveness of the

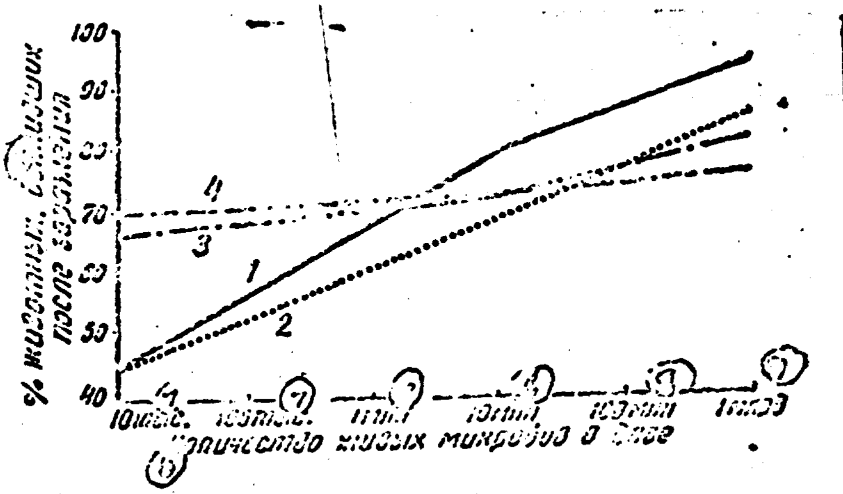

Fig. 1. Survival of Vaccinatod Guinea Pigs as a Function of the Number of Living Microbos in the Vaccine Doso (Infection with 200 CLD of a Virulent Strain). 1. Intradermal Method of Vaccination; 2. Subcutanoous Method; 3. Percutaneous Method; 4. Porcutanoous Mothod in our Modification; 5. Percent of Animals Surviving After Infoction; 6. Number of Living Microbos in the Doso; 7. Thousands; 8. Million (s); 9. Billion.

vaccine.

These principles give us reason for revising existing instructions on the preparation and application of dry living bivalent plague vaccine. We can express ourselves in favor of the advisability of calculating the single dose by the number of living microbes, which should be the same in each dose of vaccine.

In considering the effectiveness of the vaccination method note should be made (as is seen in Table 1) that with small vaccinating doses the methods of percutaneous and intradermal vaccination were most effective in our modifications; in the cases of moderate and large vaccinating doses all the methods studied gave a good vaccination effect.

For the purpose of simplifying the vaccination technique and reducing the degree of local and general reactions to the inoculation and preserving a certain measure of standardization in the vaccine dosage we recommend the new method of intradermal vaccination by means of the instrument described above. In the vaccination of experimental animals and people by this method it was noted that in the inoculees there are

57

Tablo 1.

Survival Rate of the Animals After Infection With 200,000 CLD of a Virulent Strain of Plague Microbe After Vaccination With Different Doses and Series of Vaccine and Different Methods.

(1) № группы	(2) % выживаемости вакцины (серия)	(3) Общее количество живых и мертвых микробов в дозе	(4) Выживаемость животных (в %), вакцинированных разными методами после заражения 200 тыс. Dcl			
			(5) внутрикожно		(8) накожно	(9) подкожно
			(6) шприцем	(7) нашим прибором		
(10) При содержании 10 тысяч живых микробов в дозе						
1	11,7	100 тыс.	10	50	60	0
2	30,9	30 „	50	80	50	40
3	47,9	20 „	80	80	80	80
4	100	10 „	40	70	80	60
(11) В среднем			45,0	70,0	67,5	45,0
(12) При содержании 10 млн. живых микробов в дозе						
5	11,7	100 млн.	70	70	70	40
6	30,9	30 „	80	75	60	80
7	47,9	20 „	90	75	70	70
8	100	10 „	80	70	90	90
(11) В среднем			80,0	72,5	72,5	70,0
(13) При содержании 1 млрд. живых микробов в дозе						
9	11,7	10 млрд.	100	80	80	90
10	30,9	3 „	80	60	60	90
11	47,9	2 „	100	80	90	80
12	100	1 „	100	90	100	90
(11) В среднем			95,0	77,5	82,5	87,5

1. No of Group; 2. Survival Rate of Vaccine (Series); 3. Total No of Living and Dead Microbes in the Dose; 4. Survival Rate of Animals (in %) Vaccinated by Different Methods After Infection with 200,000 CLD; 5. Intradermally; 6. With a Syringe; 7. With Our Instrument; 8. Percutaneously; 9. Subcutaneously; 10. With a Content of 10,000 Living Microbes in the Dose; 11. Average; 12. With a Content of 10,000,000 Living Microbes in a Dose; 13. With a Content of 1,000,000,000 Living Microbes in a Dose.

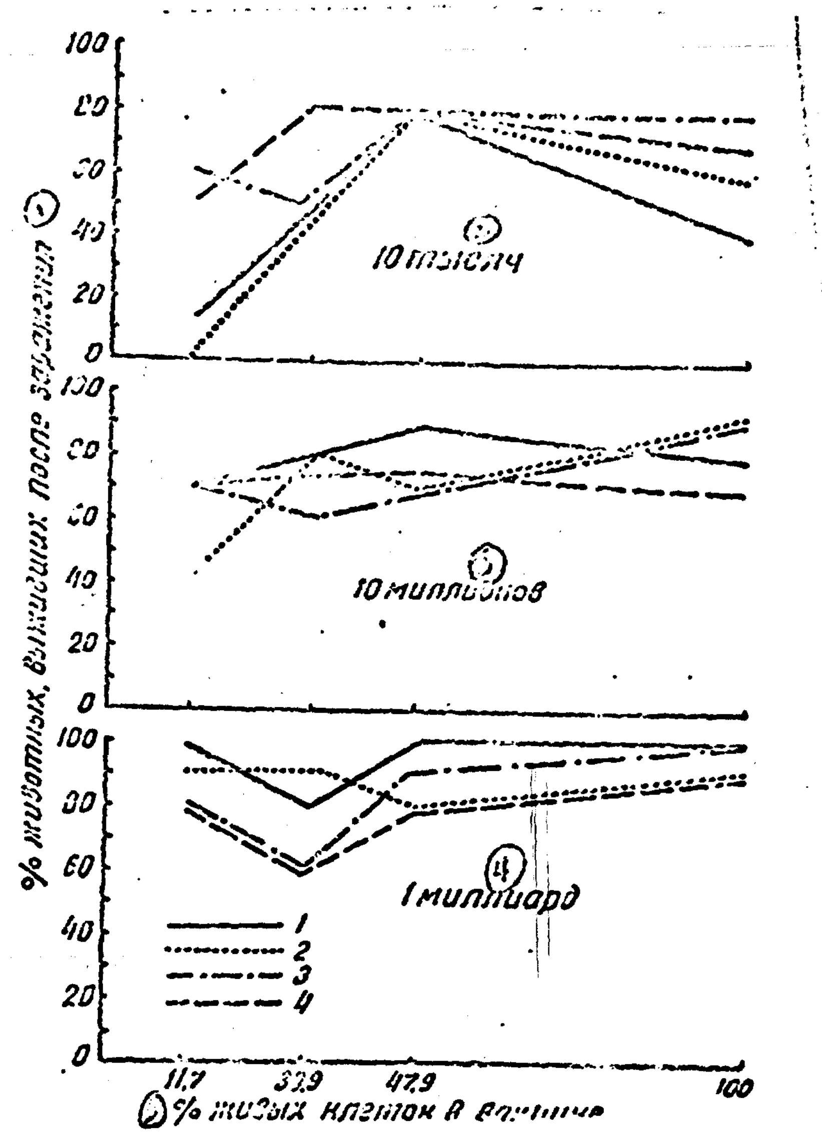

Fig. 2. Effectiveness of Vaccination of Guinea Pigs Depending on the Number of Living Microbes in the Vaccine with Different Vaccine Doses (10,000, 10,000,000, 1,000,000,000). 1. % of Animals Surviving after Infection; 2. 10,000; 3. 10,000,000; 4. 1,000,000,000; 5. % of Living Cells in the Vaccine.

no marked local or general reactions to the inoculation characteristic of the intradermal method. Our modification of the intradermal method is technically simpler than intradermal injection of the vaccine with a syringe and even simpler than per cutaneous vaccination, and the postvaccinal immunity obtained is not inferior in its strength to immunity obtained from ordinary intradermal vaccination. In addition, in our method the vaccine can be dosaged more accurately than by the percutaneous method.

Conclusions

1. Vaccine with a high survival rate is more effective than vaccines with low survival rates.

2. Vaccine series with low (11.7) and very high (about 100) survival rates possess greater side-effect production than vaccines with an average survival rate (30.9 and 47.9).

3. The variant of the intradermal method of vaccination which we have proposed is no less effective than intradermal (classic) and percutaneous methods, is technically simple and may be recommended for comparative testing on a large scale.

4. Extensive study is necessary of the effectiveness and side-effect production of different dosages of vaccines with different survival rates on people with the aim of clarifying the optimum dosages for each method of vaccination.

pp 437-451

The Current Status of the Study of the Epizootology of Tularemia in the USSR

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Since cases of tularemia began to be diagnosed in the USSR (Suvorov, Vol'ferts and Voronkova, 1926) medical workers have directed attention to the demonstration of sources of infection. It has been determined that the source of the infection consisted of water rats [Arvicola terrestris] (Golov, Knizevskiy, Berdnikov and Tiflov, 1928; Zarkhi, 1929), small mouse-like rodents (Kazantseva and Gorokhov, 1934; Berdnikov, 1934; Semov, 1934), hares (Berezin, 1931). In 1930, for the first time cases of arthropod origin were detected (Sinay and Popov; Krol'). In 1934, the possibility was determined of infection from water (Semov, Vol'ferts and Novikova).

In subsequent years through the work of a number of expeditions (VIEM [All-Union Institute of Experimental Medicine], TIEM [Institute of Epidemiology and Microbiology], the "Mikrob" Institute, and the Rostov Plague Institute) and various laboratories new species of warm-blooded animals and arthropods were found which were spontaneously infected with tularemia bacteria. Through the work of zoologists and parasitologists the relationship was made clear between the development of mass epizootics among rodents and their census, and the important role of blood-sucking diptera and ixodial ticks was determined in the transmission of the tularemia pathogen. For some of the foci the significance of ixodial ticks as reservoirs of the tularemia microbe was shown in the interepizootic period. In 1943, the knowledge gained by Soviet investigators in the study of tularemia during this period was generalized on in the book Tularemia Infection, published under the editorship of L. M. Khatenover.

Subsequently, because of the comprehensive work of bacteriologists, parasitologists and zoologists, who made both field and experimental investigations the main problems of the epizootology of tularemia were solved in the Soviet Union. An important step was constituted by work on classification and study of foci of tularemia, elucidating their structure and characteristics of the existence of the infection in them (Maksimov, 1946; Olsuf'yev, 1946; Kuzyakin, 1947; Bozhenko, 1950; Lebedev, 1953; Karpov, 1955; Kucheruk, 1955; Myasnikov, 1955, and others).

Underlying the classification of natural foci of tularemia are epizootological and epidemiological differences observed under the conditions of different landscapes. In accordance with this principle the best accepted form is the distinction of foci according to landscape

characteristics with consideration of the basic species of animals providing for the circulation of the pathogen in the focus.

With the investigation of the natural foci of tularemia in different regions of the Soviet Union, the number of types of foci described is increasing. V. P. Bozhenko (1956) points out, for example, that the number of types of foci described reaches 20. In the description of foci of tularemia at the present time authors do not always adhere to a single classification principle along with the landscape principle of classification works are encountered which describe the "rat" type, "water" foci, "hamster" focus, etc. Excessive fragmentation is observed in distinguishing types of foci, for example, river valley, delta, bog water, river, etc. There are synonyms in the definition of foci of the same types.

Recently, attempts have appeared to put order into the classification of types of foci. V. P. Bozhenko (1956), in distinguishing seven basic types of foci (river valley, delta, mountain-valley, bog water, meadow-field, forest and steppe), suggests combining them into two groups: I-- water foci, where the main reservoir is the water rat, and II-- foci of dry landscapes. The last group includes meadow-field, forest, and steppe types of foci, which is hardly justified.

N. G. Olsuf'yov suggests keeping the division into five basic landscape types of foci (tidal marsh, meadow-field, steppe, forest and foothill-brook), regarding the various foci included in the major landscape subdivisions as modifications or variants of them. For example, the river valley type of focus, characterized by the participation of the water rat in the circulation of the pathogen, includes the delta and other variants. In the steppe type of focus the "ravine" (Borodin, 1956) and "hamster" (Bozhenko, 1955) variants are included.

A. A. Maksimov (1956) suggests dividing the basic type of foci into extremely small variants, giving them a purely landscape characterization without consideration of the specific epizootological conditions of existence of the infection in them. For the purpose of putting problems of classification of the foci in order it is desirable to make a more thorough study of the structure of the foci, investigation of the lines of circulation and preservation of the pathogen in them on the basis of a study of the elementary foci of infection. Of basic significance for understanding the conditions under which the tularemia pathogen circulates in nature is the termination of the virulence of the natural (focal) strains. Study of the biological properties of strains of Bacterium tularense isolated in different natural foci from various animals and environmental objects has shown that highly virulent focal or epidemic strains circulate in nature. The virulence of a large number of strains, checked by the method accepted at present (by titration of dilutions of suspensions of a culture of tularemia bacteria in white mice, white rats and guinea pigs) has turned out to be very much the same. A full lethal dose for white mice and guinea pigs is equal to one microbe (according to the bacterial standard of the TsGNKI /Central State Scientific Testing Institute/); for white rats the full lethal dose is equal to 100,000,000

-1,000,000,000 microbes. As is seen from Table I, strains isolated at the beginning and at the end of the epizootic from sick animals found sporadically, ixodial ticks, water, and from substrates making up ricks and straw stacks have the same virulence characteristics (Olsuf'yev, Yemel'yanova, Pom...skaya, K...olova, S...onova).

Other investigators (Mashkov, 1949; Filipenko, 1953; Bozhenko, 1955; Sorina, 1955), checking the virulence of strains of tularemia microbe on white mice, also noted the high degree of virulence of all the strains isolated.

We know of only one reliable example of variation in the tularemia pathogen under natural conditions: its higher virulence on the American continent by comparison with that on the territory of Asia and Europe. However, these differences are undoubtedly associated with the prolonged evolution of the pathogen under different existential conditions on different continents (Olsuf'yev, 1956).

Experimental study of the variation in the tularemia microbe has confirmed the absence of a change in virulence in the natural route of spread and maintenance of the pathogen (Yemel'yanova). Repeated passages through guinea pigs and white mice of strains isolated from ixodial ticks (strain No. 503; 360 passages) and the body of the common vole (strain No. 9; 500 passages) accomplished in the laboratory of tularemia of the ... for seven years did not change the characteristics of the strains. Prolonged maintenance of tularemia microbes in the environment did not ... any reduction of virulence either. According to the observations of O. S. Yemel'yanova (manuscript) and L. A. Lomanskaya (1956), the finding tularemia bacteria in the environment causes a gradual extinction of the microbes. With the isolation of tularemia microbes which have been preserved for a long time in the environment (in water, soil, on grain, ... on straw) an increase in the survival time is observed in the biological test animals and a delayed growth of the culture on direct inoculation. These phenomena, which have been taken by some investigators as an indication of reduction of virulence, are caused by an increase in the lag-phase of such aging cells which have not multiplied for a long time (Yemel'yanova).

The passaging or prolonged preservation of tularemia bacteria in the bodies of slightly susceptible animals (among different species of rodents and insectivores as well as in frogs) does not change the virulence of the strains (Yemel'yanova, Zinina). Nor has any reduction been noted after prolonged stay of bacteria in the bodies of immune animals--souslikss, voles, guinea pigs (Olsuf'yev, Dunayeva, Yemel'yanova and Savel'yeva). Prolonged preservation in ixodial ticks does not exert any effect on the virulent properties of the microbe either (Olsuf'yev and Petrov, 1953). An illustration of what has been stated is given in Table II.

For many years at all the tularemia (as well as plague) stations, a method of investigating rodents and arthropods was used which was entirely suitable for isolation of strains with reduced virulence (two or three or more passages were made and inoculations ... made on egg yolk

Table I

Virulence of Strains of Tularemia Microbe Isolated in Natural Foci According to the Data of the Tularemia Laboratory of the IEM imeni Gamaleya of the Academy of Medical Sciences USSR

Место выделения штамма (1)	(2) № штамма	(3) Объект, из которого выделен штамм	(4) Время выделения	Результат заражения лабораторных животных разными дозами (в микробных клетках) (5)						
				(6) белые мыши			(7) белые крысы			
				0,1	1	10	1 млн	10 млн	100 млн	1 млрд (17)
Пойма Оки (8)	21	Полевка обыкновенная (9)	III 1948 г. (16)	−++ 77	+++ 777	+++ 766	−−	—	++ 33	++ 32
	6	Мышь-малютка (10)	XII 1948 г.	+++ 777	+++ 776	+++ 666	−+ 8	−−	++ 33	+ 3
	120	Полевка обыкновенная (11)	III 1949 г.	+++ 877	+++ 666	+++ 665	−+ 4	++ 44	−+ 4	++ 34
	21	Водяная крыса (12)	VII 1949 г.	+++ 877	+++ 766	+++ 766	−++ 44	+++ 432	+++ 333	+++ 332
Волго-Ахтубинская пойма (14)	132	Dermacentor marginatus	1953 г.	−++ 79	+++ 876	+++ 666	+++ 12 5 3	+++ 433	+++ 632	+++ 333
	125	Rhipicephalus rossicus	1954 г.	−−−	+++ 876	+++ 766	−−−	−++ 43	+++ 333	+++ 332
Предгорный Алтай (15)	66	Водяная крыса (12)	1955 г.	−++ 88	+++ 666	+++ 666	−++ 12 7	−−+ 3	+++ 433	+++ 322
	223	Вода (13)	1955 г.	−++ 87	+++ 777	+++ 777	−−+ 3	−−+ 4	+++ 773	+++ 222
	129	Dermacentor silvarum	1956 г.	−++ 66	+++ 555	+++ 655	−−−	−−+ 7	+++ 543	+++ 432

Key: (+), Animal died of tularemia; (-) Animal survived. The number under the symbol shows the survival time of the animal in days. 1. place [illegible] isolation; 2. number of strain; 3. object from which strain isolated; 4. time of [illegible]; 5. result of infection of laboratory animals with [illegible] doses (in [illegible]); 6. white mice; 7. white rats; 8. Oka river valley; 9. common [illegible]; 10. harvest mouse; 11. same as 9; 12. water rat; 13. water;

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14. Volga-Aktyubinski river valley; 15. foothills of the Altay range; 16. million (s); 17. billion; 18. March 1948.

6964

Table II

Experimental Study of the Virulence of Strains of Tularemia Microbe (according to the data of O. S. Y[illegible]mel'yanova, R. A. Savel'yeva, V. G. Petrova and L. A. Pomanskaya)

Штамм и его характеристика 1	Результат заражения лабораторных животных разными дозами (в микробных клетках) 2					
	3 белые мыши			4 белые крысы		
	0,1	1	10	10 [illegible]	100 [illegible]	1. [illegible]
№ 9 (исходный от полевки) 7	— — — — — + 7	+ + + 7 7 6 + + 6 6	+ + + 6 6 6 + + 6 6	— — + 8	+ + + 11 6 4	+ + + 6 4 2
№ 9 ([illegible] пассажей через белых мышей) 8	— + + 3 7 + + 7 7	+ + + 7 6 6 + + 6 6	+ + + 6 6 6 + + 6 6	— + + 7 5 + + 4 3	— — + 4 + + 3 2	+ + + 3 2 2 + + 2 2
№ 503 (исходный от D. pictus) 9	— — + 6	+ + + 7 6 6	+ + + 6 5 5	— + + 8 3	+ + + 4 3 3	+ 3
№ 503 (318 пассажей через морских свинок) 10	— — + 7 + + 7 7	+ + + 8 7 7 + + 7 6	+ + + 7 7 7 + + 8 6	— — — + + + 4 3 3	— + + 3 3 + + 3 3	+ + + 3 2 2 + + 2 2
№ 503/1761 (5 месяцев в организме иммунной морской свинки) 11 . . .	+ + + 7 7 7	+ + + 7 7 6	+ + + 6 6 6	+ + + 5 6 6	— + + 5 4	+ + + 4 4 4
№ 503 700 дней в клещах D. marginatus 12	+ + + 7 7 7	+ + + 6 6 6	+ + + 6 6 6	+ + + 3 3 4	+ + + 3 3 3	+ + + 3 3 3
№ 58 (118 дней хранения на субстрате) 13 .	— + + 7 7	+ + + 8 7 7	+ + + 7 7 7	+ + 5 4	+ + + 8 5 1	+ + + 3 2 1

Key is the same as in Table I

1. the strain and the characterization of it; 2. the result of infection of laboratory animals with different doses (in microbes); 3. white mice;

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4. white rats; 5. millions; 6. billion; 7. original from vole; 8. 500 passages through white mice; 9. original from D. pictus; 10. 318 passages through guinea pigs; 11. 5 months in the body of an immune guinea pig; 12. 700 days in D. marginatus ticks; 13. 143 days on a substrate.

medium). Despite this, freshly isolated strains with low virulence were not obtained anywhere or described according to the accepted method. The isolation of highly virulent strains of the tularemia microbe (Olsuf'yev and Yermolova, 1955) by direct inoculation from ixodial ticks (Dermacentor marginatus) once again confirmed the conclusion that in nature highly virulent strains of tularemia bacteria circulate which have preserved their properties in a stable manner with natural spread of the pathogen.

Finally, experimentally the impossibility of spread of bacteria of a vaccine strain has been shown among highly susceptible animals (common vole, steppe lemmings /Lagurus lagurus/ and white mice) either with close contact of infected and healthy animals or through ectoparasites, ixodial ticks (Dunayeva).

In cultivation on synthetic nutrient media in laboratories the virulence of the strains is reduced (Yemel'yanova, 1950). For the purpose of demonstrating the initial stage of attenuation of strains of the tularemia microbe it is necessary to use infection of guinea pigs and white rats, because white mice die of tularemia even after administration of minimum doses of a dissociated culture because of their high degree of susceptibility to infection. According to the data of M. I. Tereshchenko and N. G. Olsuf'yev (1956), strain No. 9, isolated from the vole in December 1943 and kept in a museum under refrigerator conditions (+ 4°) with subcultures every 30-45 days after four years decreased in virulence for white rats and guinea pigs, whereas for white mice one microbe remained the full lethal dose after subcutaneous administration, except that the mice died later. The same strain, maintained for four years by passages through white mice, preserved its original virulence for all three species of animals.

Despite the high degree of susceptibility to infection of the white mice, infection of them with museum strains possessing reduced virulence for white rats and guinea pigs causes an infection in mice which is qualitatively different from tularemia produced by infection with highly virulent cultures.

The disease is longer lasting, is not accompanied by massive septicemia characteristic of tularemia in animals of the first group (see below), but rather is characterized by a considerable reduction in the number of microbes in the organs of mice and particularly in the blood.

In Table III the results are presented of infection of white mice with a culture of the tularemia microbe, strain No. 1254 at various periods after its isolation. The strain was isolated by workers of the Stavropol' plague station from the body of a house mouse in 1948 and was kept in a museum, with subcultures made on coagulated egg yolk medium.

Table III

Results of Infection of White Mice with Strain No. 1254 of the Tularemia Microbe Isolated in 1943 and Kept in the Museum of the Stavropol' Plague Station (According to T. N. Dunayeva)

(1) Доза в микробных клетках	(2) Число мышей: (3) всего	(4) из них пало	(5) Сроки гибели в сутках	(6) Бактериоскопия в баллах: (7) селезенка	(8) кровь
(9) Опыт 31 августа 1950 г.					
0,1	7	2	7,7	(11) III у обеих мышей	(15) II и III
1	9	9	0,6,7,7,7,7,7,8,8	(12) III у 2 и IV у 7 мышей	III у 5 и IV у 4 мышей (14)
10	10	10	6,6,6,6,6,7,7,7,7,7	(13) III у 2 и IV у 8 мышей	III у 5 и IV у 5 мышей (16)
(10) Опыт 30 мая 1951 г.					
0,1	5	1	10	0	0
1	5	5	8,8,8,10,10	(17) 0 у 2, II у 2 и III у 1 мыши	0 у 5 мышей (19)
10	5	5	8,8,8,10,10	(18) 0 у 2, II у 1 и III у 2 мышей	0 у 3 мышей (20) II у 2 мышей (21)

1. dose in microbes; 2. number of mice; 3. total; 4. number of them which died; 5. time of death in days; 6. bacterioscopy in pluses; 7. spleen; 8. blood; 9. experiment 31 August 1950; 10. experiment 30 May 1951; 11. +++ in both mice; 12. +++ in 2 and ++++ in 7 mice; 13. +++ in 2 and ++++ in 8 mice; 14. +++ in 5 and ++++ in 4 mice; 15. ++ and +++; 16. +++ in 5 and ++++ in 5 mice; 17. 0 in 2, ++ in 2, and +++ in 1 mouse; 18. 0 in 2; ++ in 1 and +++ in 2 mice; 19. 0 in 5 mice; 20. 0 in 3 mice; 21. ++ in 2 mice.

In the summer of 1950 the strain still preserved its virulent properties. Its CLD for animals of the first group amounted to one microbe (according to the TsGNKI standard). The animals died with active bacteriemia. In all, 180 animals of the first group were infected (house mice of a wild and of a laboratory race, wood mice, common voles, gray hamsters [Cricetulus migratorius], and other hamsters [Cricetus raddei and Cricetus cricetus]). For dwarf sousliks [Citellus pygmaeus] the CLD amounted to 1,000,000,000 microbes; part of the animals died of a dose of 10,000,000-100,000,000 (Dunayeva and Pshenichnaya, 1953). For forest dormice [Dyromys nitedula] the dose was equal to 100,000,000; part of the

animals died of doses of 100,000-1,000,000 microbes.

In 1951 the virulence of the strain decreased. White rats did not die after infection with doses of 10,000,000 or 100,000,000 microbes (three rats per dose), but they died on the third and fifth days from a dose of 1,000,000,000 microbes. Although the CLD for white mice amounted to one microbe, the duration of the disease in them was considerably increased, and the development of the infection was not associated with massive septicemia. Of the 11 mice which died microbes were not found bacterioscopically in the blood of nine mice, and only in two mice were a small accumulation and isolated microbes found in the blood, which are not at all characteristic of animals of the first group infected with entirely virulent cultures of tularemia bacteria.

Increase in the duration of the disease and the marked reduction of the intensity of septicemia are evidence to the effect that the protective forces of the bodies of white mice are capable of limiting partly the multiplication of tularemia bacteria with reduced virulence.

In animals of the first group the nature of the course of tularemia caused by museum strains depends on the degree of dissociation of the strain and variations in the individual susceptibility of animals associated with species, age, seasonal and other physiological characteristics of the organism (Kalabukhov, 1949; Volchanetskaya, 1953).

In a manner similar to the problem of the virulence of strains of the tularemia microbe many problems in the epizootology of tularemia have been solved experimentally and in combination with field observations.

Spontaneous infection with tularemia has at the present time been found in 48 species of wild mammals, including 36 species of rodents, five species of insectivores and seven species of carnivores.

The abundance of species of animals infected with tularemia under natural conditions required a determination of their epizootological significance. On the basis of an experimental study of the characteristics of the course of tularemia in more than 50 species of wild animals (rodents, carnivores and insectivores) three groups of animals were distinguished which were different with respect to the degree of susceptibility and sensitivity to this infection (Olsuf'yev, Dunayeva and others, 1950).

First group-- animals highly susceptible and highly sensitive to tularemia, in which infection with isolated bacteria causes the development of a lethal infection. In this group are all the mice in Soviet fauna with the exception of field mice, hamsters, voles, sand rats, hares, shrews, moles and others.

Second group-- animals which are highly susceptible but not very sensitive to tularemia. The animals are infected and become sick with tularemia after the subcutaneous injection of one microbe; death is caused usually only by massive doses, of 10,000,000-100,000,000 microbes and even higher. Having tularemia leads to a more or less prolonged bacterial carriage (from 20 to 40 days, and less often, longer) and is responsible for the production of immunity, at first, not a sterile immunity and then sterile immunity. This group includes the following:

field mouse, all rats of Soviet fauna (of the genera Rattus and Nesokia), sousliks, the long-toed souslik [this is an error: there is a long-tailed souslik and a thin-toed souslik, but not a long-toed souslik], squirrel, chipmunk, beaver, hedgehog, desman, water shrew, and the small shrew Suncus etrusca and others.

Third group-- animals which are not very susceptible and practically insensitive to tularemia. This group includes various representatives of the order of carnivora: foxes, Ussuriysk racoons, polecats, weasels, the ermine, domestic cat and dog.

The degree of susceptibility and sensitivity to infection is a species characteristic which does not undergo any essential changes in accordance with age of the animals or season of the year (Dunayeva and Olsuf'yev, 1953; Dunayeva, 1954; N. and Ye. Makarovy and Bagayeva, 1955; Kamolova, in the press; Bystrova, in the press).

The features of the course of the infectious disease characterizing each group are of decisive importance for determining the epizootological significance of the animals.

Under the same conditions of infection the intensity of septicemia in animals of the first and second groups is very much different. By titration of suspensions of infected animal organs on white mice it is possible to establish the intensity with which various organs are seeded according to days of infection (Fig. 1).

In animals of the first group after a brief adaptation phase (corresponding to the lag phase of multiplication of bacteria) the multiplication of tularemia bacteria proceeds in a logarithmic progression as early as the second day after infection. At this time, the number of bacteria doubles (time of generation-- g) every 3.5 hours (Tereshchenko and Olsuf'yev, 1956; Dunayeva). The logarithmic phase of multiplication lasts for the entire infectious process and terminates shortly before death of the animal, accounting for the mass seeding of all organs and of the blood with bacteria. The intensity of seeding of the spleen and blood of animals of the first group (house mice, harvest mice, common voles, social voles [Microtus socialis], bank voles [Clethrionomys glareolus], steppe lemmings [Lagurus lagurus], water rats and gray hamsters) which died after infection with both small and large doses of tularemia pathogen amounts to 10,000,000,000-100,000,000,000 microbes per gram of tissue or per cc of blood (Dunayeva). These characteristics of the course of the infectious disease account for the dissemination of microbes in the excretions and transmission of them through the blood by ectoparasites (Olsuf'yev, Dunayeva and others, 1950; Dunayeva, 1954).

In animals of the second group the adaptation phase of the microbes at the site of injection is more prolonged, and they penetrate into parenchymatous organs only on the third day (after infection with 10 microbes). The logarithmic phase of multiplication of bacteria in the bodies of animals of the second group lasts a total of about two days. The intensity of seeding at the height of development of the infection comes to a total of 1,000,000 microbes per gram of tissue. Even on the sixth day, under the influence of the development of immunological

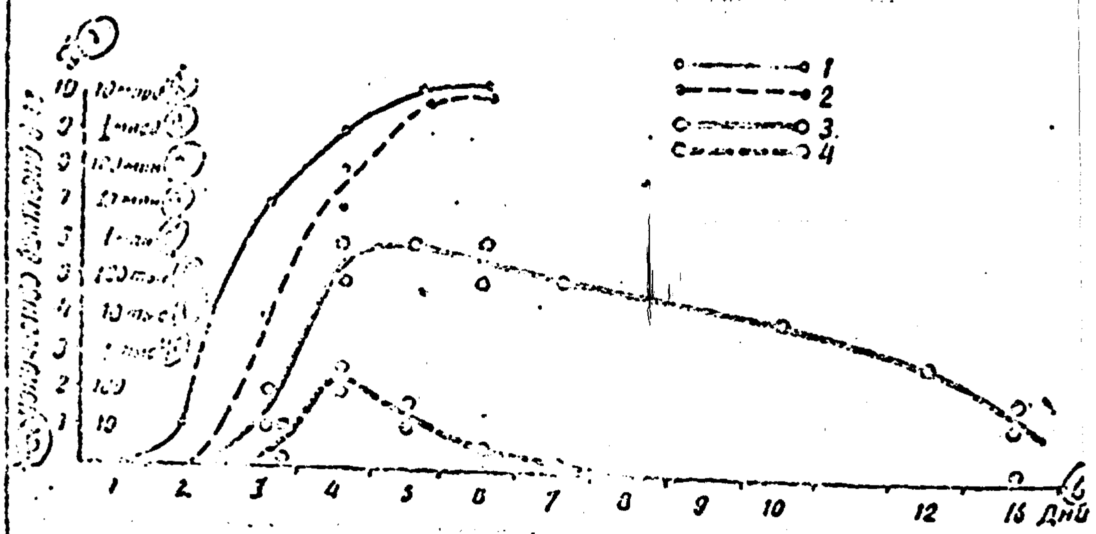

Fig. 1. Intensity of Seeding of Tularemia Bacteria on One Gram of Spleen Tissue and Blood of Animals of the First (Common Vole) and Second Group (White Rat) after Infection with a Dose of Ten Microbes of a Virulent Strain, No. 503. 1. spleen of vole; 2. blood of vole; 3. spleen of white rat; 4. blood of white rat; 5. number of bacteria per gram; 6. days; 7. log; 8. billion (s); 9. million (s); 10. thousand (s).

reactions of the body a reduction occurs in the intensity of seeding of the organs with bacteria, which lasts for the entire period of decline of the infection (Fig. 1). In accordance with the comparatively low level of bacterial seeding of the basic foci of multiplication (spleen, liver) the entrance of bacteria into blood of animals of the second group is hundreds of thousands times less than in animals of the first group. The largest number of bacteria in the blood of field mice and white rats after infection with 10 microbes amounted to a total of 500 microbes as against 10,000,000,000 microbes in animals of the first group. For species of the second group a slight or moderate bacteriemia is characteristic even in the fatal cases, produced by infection with massive doses of the pathogen: 100,000,000-1,000,000,000 microbes. On account of these developmental characteristics of the infectious disease, the infection of blood-sucking vectors of animals of the second group is made difficult and occurs only sporadically. The small number of bacteria which enter the ticks in such cases does not always assure transphasic transmission of the pathogen (Petrov and Dunayeva, 1955).

On the basis of experimental investigations, in complete agreement with epizootological observations in nature, the significance of species of the second group is considered secondary. In the majority of cases

animals not very sensitive to tularemia are blind alleys for the infection, and they cannot independently, without participation of animals in the first group, maintain the existence of natural foci of tularemia (Olsuf'yev, Dunayeva and others, 1950; Dunayeva, 1954). The idea that certain species of the second group (sousliks, chipmunk) are of epizootological importance and play a role of some importance in the formation of tularemia foci, which has been expressed by N. I. Makarov and Ye. P. Makarova, O. K. Kupressova and F. S. [illegible] (1956), underestimates the significance of the quantitative characteristics of development of the infection in animals and the relationship of the infectivity of the sick animal to the intensity of bacteriemia.

Species of the third group are not of any importance as sources of infection. Their sanitary significance should rather be noted, because the role of the carnivores making up this group in eradicating accumulations of rodents is very great, and in many cases they can exert a restrictive influence on the spread of an epizootic by catching sick animals.

With respect to the role of arthropod vectors in the epizootology of tularemia it has been shown by field observations and experimental studies that ixodial ticks are of leading significance as vectors and long-term reservoirs of tularemia bacteria (Golov, Olsuf'yev, Bozhenko, Petrov). While previously the significance of ixodial ticks was proved only for foci of the foothill-brook (Golov, 1934) and meadow-field types (Olsuf'yev, 1943) in maintaining the existence of the infectious disease, at the present time their participation in the circulation of the pathogen has been demonstrated in all types of foci studied. The river valley type of focus (with its delta variant) does not constitute an exception in this case, which is evidenced by the results of investigations made in the Oka river valley and Volga-Aktyubinsk valley (Olsuf'yev and coauthors) and in the Don delta (Bozhenko, Romanova, 1955). For the Volga delta V. B. Dubinin (1953) notes a number of species of ticks which are known as tularemia vectors, while V. G. Pilipenko and K. P. Derevenchenko (1955) found Hyalomma plumbeum ticks infected with tularemia bacteria on a hare.

Concerning the role of other species of vectors at the present time the following is known: mosquitoes (Aedes, Culex, Anopheles), being mechanical vectors of the tularemia pathogen, are of essential epizootological and epidemiological significance in the spread of tularemia in the river valley type of focus. Attention should be directed at the duration of preservation of tularemia bacteria in mosquitoes at low temperature. Horseflies can also be vectors but no more than two or three days after feeding on an infected animal (Olsuf'yev, 1943; Bozhenko, 1936). Fleas are also of limited significance as agents for spreading tularemia among animals, because transmission through the bite of the flea is made difficult (Sazonova, 1953; Dudolkina, 1954). Lice of rodents (Hoplopleura) may be of importance in spreading the infection in a crowded settlement of animals, for example, in ricks.

With respect to gamasid ticks it should be noted that inadequate

knowledge about this group of parasites (their classification and biology), the small number and inadequacy of experiments made have rendered the elucidation of their epizootiological significance difficult (Zokhvatkin, 1948). Recently, Ye. N. Nel'zina (1957) did very interesting work, showing that some species of the genus Hirstionyssus (H. isabellinus, H. musculi, H. criceti), which are obligate hematophages, are capable of transmitting the infection to animals (white mice) at the time of blood sucking. Transmission of bacteria was accomplished through the feeding of a single tick. These data as well as facts about the preservation of tularemia bacteria in the bodies of gamasid ticks up to 47 days (Pilipenko, 1953) and 108 days (Nel'zina) show that some species of gamasid ticks can be of importance in spreading the tularemia pathogen. It is entirely possible that gamasid ticks specifically are responsible for the occurrence of tularemia epizootics among the common voles and house mice in the autumn, the cause of which has remained unclear.

Of greatest importance in the epizootology of tularemia is the problem of the mechanism of preservation of the pathogen in the interepizootic period. So far there is no agreement as to the solution of this problem. Developing the hypothesis expressed in 1928 by D. A. Golov and co-workers and supported after that by B. V. Voskresenskiy and N. V. Nikipelov, a number of authors believes that the existence of the tularemia pathogen in nature can be maintained by tularemia with a latent or chronic course in animals of the first group: water rats, common voles, muskrats and others (Sveshnikova, 1950; Pilipenko, 1953; Karpov, 1954). The scheme of circulation of the pathogen proposed by the authors assumes the possibility of a relatively rapid change in the virulent properties of the microbe and the capacity of tularemia bacteria to remain for a long time in the bodies of water rats and other highly sensitive animals without causing clinical signs of the disease. Recently, V. P. Bozhenko (1956) as well as G. A. Kondrashkin and L. I. Kuznetsova (1956) have come out to support this conception.

These ideas contradict factual data about the properties of the tularemia microbe, the rules and regulations of the pathogenesis of tularemia in animals of the first group and the epizootological materials confirming the role of ixodial ticks as long-term reservoirs of the microbe in all the tularemia foci studied and the fact of the negligibly low degree of infection of water rats in the interepizootic period. I should like to mention that V. G. Pilipenko (1953) points out that for three autumn-winter interepizootic seasons a total of three cultures of tularemia microbe was isolated from the investigation of 16,000 water rats. In the Volga-Aktyubinsk river valley 14,000 water rats caught in 1952-1955 were investigated with negative results, whereas 38 strains of the tularemia pathogen were isolated here in the same period from D. marginatus and Rh. rossicus ticks (Olsuf'yev, Petrov, Yanolova and others, 1954; Yanolova, Val'kov, Murav'yeva and others, 1956).

For the purpose of studying the problem of the possibility of the chronic course of tularemia in animals of the first group, T. N.

Dunayeva made special experiments in which there were 426 animals under observation (this included 98 water rats, 233 common voles, 46 steppe lemmings, 16 harvest mice, 34 white mice) which survived in an experimental observation. In the experiments strains of tularemia microbe with typical virulence were used, freshly isolated or kept in the laboratory by means of continuous passages through animals.

Different methods of infection were used: subcutaneous, intradermal, alimentary, and by means of feeding infected nymphs of ixodid ticks (D. marginatus and Rh. rossicus) on rodents. In the case of subcutaneous and intradermal infection the animals regularly died from a dose of one microbe or more. After the administration of further dilutions of a suspension of the culture corresponding to doses of 0.5, 0.2 and 0.1 microbe by the optical bacterial standard, part of the animals survived. On alimentary infection the common voles all died from a dose of 1,000,000 microbes, while the majority of the voles survived after smaller doses (1,000-100,000 microbes). Feeding of a single infected nymph on the voles caused death of only part of the individuals. The infection of the nymphs was determined by subcutaneous administration of a suspension of a nymph which had fallen off into white mice.

The animals were under observation one to three months. For purposes of provocation of tularemia in them different factors weakening them were used-- chilling with soaking, inadequate nutrition, starvation, as well as infection with sublethal doses of pathogens of other infectious diseases-- erysepeloid and Bacillus breslau paratyphoid fever. In no case was provocation of the tularemia infection obtained, but bacteriological, serological and immunological investigations did not reveal either bacterial carriage in the animals or other traces of the disease.

The experiments of N. S. Yamolova (in publication) made on 139 water rats which survived after the administration of "sublethal doses" of tularemia bacteria also failed to reveal any latent infection in them. The same results have been obtained by M. P. Tereshchenko (1956) in experiments with house mice (there were 120 animals under observation).

The differences in the experiments of these authors and the experiments of L. I. Kuznetsova (1956) and V. P. Bozhenko and S. F. Shevchenko (1956) are explained apparently by the use of museum strains by the latter authors which have lost some of their virulence as the result of cultivation on synthetic nutrient media.

I should like to mention that McCoy and Chapin (1912) noted that cultures of the tularemia microbe produce an infection with a chronic course in guinea pigs after 7-12 subcultures on egg yolk medium, which is not observed after infection with freshly isolated strains. American investigators have maintained the virulence of strains of tularemia pathogen by passages in animals. Thus, for example, the Schu strain, isolated from a sick person in 1941 has maintained its original characteristics to the present time.

With respect to bacterial carriage in animals of the second group which have had tularemia, it has been determined that it is not of definite epizootological significance, because it is associated with the

development of a strong immunity which prevents provocation of the infection to a generalized form (Yyseli, 1951; Dunayeva, 1954).

On the basis of a detailed study of different types of foci in combination with experimental investigations a group of investigators headed by N. G. Olsuf'yev believes that the tularemia pathogen under natural conditions and with natural circulation through warm-blooded animals and arthropods and when it stays in the environment does not at present undergo essential changes in its biological properties, including virulence. Of primary significance in the formation and preservation of virulent properties of the tularemia microbe is the mechanism of transmission, which is accomplished in nature chiefly through blood-sucking arthropods, for the infection of which mass seeding of the blood of the animal donors is necessary. The absence of the phenomenon of bacteriophagia also limits the range of variation in the tularemia bacteria.

Prolonged existence of natural foci of tularemia for many years is maintained chiefly by ixodial ticks (of the genera Dermacentor, Ixodes, Rhipicephalus, and Haemophysalis), which during their entire lives and throughout the course of metamorphosis preserve tularemia bacteria in themselves and in this way carry the pathogen from season to season and from year to year. An important biological characteristic of the interrelations between the ticks and the tularemia pathogen is the active multiplication of bacteria in the body of the tick during blood-sucking on animals, which provides for an increase in infection of the tick by hundreds of thousands of times in going from the larva to the imago.

With respect to transovarial transmission of tularemia bacteria in ticks there are indications by N. G. Olsuf'yev (Olsuf'yev and Tolstukhina, 1941) which have not been confirmed in the experiments of other authors. Thus, D. A. Golov (1935) showed through extensive material the absence of transovarial transmission of tularemia bacteria in D. marginatus ticks. In the experiments an investigation was made of 7,663 larvae and 462 nymphs obtained from infected females. Feeding of the larvae and the nymphs was carried out on water rats and common voles. T. N. Dunayeva investigated the eggs of 787 larvae and 142 nymphs bred from infected D. pictus females with negative results. Negative results were obtained by Ya. F. Shatas and N. A. Bystrova (1954) who investigated the eggs of 550 larvae, 320 nymphs and 170 imagoes bred from infected females. Negative results were also obtained in the experiments of S. F. Shevchenko, who investigated 1,965 larvae and nymphs of Rh. rossicus obtained from infected females.

V. P. Romanova and V. P. Bozhenko (1956) report that D. marginatus ticks are capable of transmitting the tularemia pathogen transovarially. Whereby, no transmission of bacteria was observed by larvae at the time of blood-sucking, although 18,800 larvae were fed on 94 white mice. In the investigation of 2,100 larvae by means of inoculation of 70 white mice four positive experiments were obtained. The feeding of 1,000 nymphs on 50 white mice caused disease and death from tularemia in two

mice, and in the investigation of a suspension of 240 nymphs on 48 white mice four mice died of tularemia. Mature ticks (330 females) did not transmit the infection at the time of feeding on guinea pigs (10 ticks per guinea pig). On the investigation of a suspension of 135 satiated ticks (three ticks per biological test) tularemia bacteria were found in two biological tests.

These data show that while transovarial transmission is encountered, though rarely, the number of bacteria being transmitted to the offspring is so small that even when they multiply during a period of blood sucking of the ticks adequate infection of the latter is not produced sufficient for regular transmission of the bacteria.

What has been presented above shows that there has been a considerable lag in the final development of this problem. Apparently, the statement is more reliable that in ticks transovarial transmission of tularemia bacteria is of no practical significance in the epizootology of tularemia.

The transmission of the pathogen from ticks to the animals is accomplished by nymphs (infected in the larval stage) and by mature individuals of the ticks the imagoes of which feed on animals highly sensitive to tularemia. In this connection hares and hamsters, which feed all the phases of some species of ticks, deserve the greatest attention. Of importance in the spread of tularemia bacteria are ticks living in rodent holes, Ixodes laguri, I. apronophorous, I. trianguliceps, which in all phases of development are parasitic on small wild animals (rodents).

Consideration should also be given to the possibility of effective transmission of the infection by some species of gamasid ticks and lice. It should be emphasized that despite the great adaptation of the tularemia microbe and the finding of tularemia in a large number of species of mammals (about 48 species) spread of the infection among them is usually not so active as might be expected. It is perfectly obvious that definite conditions are necessary for the existence of the infectious disease and for its extensive spread over a territory.

The intensity of spread of the tularemia infection among a multitude of susceptible species of animals depends on the degree of sensitivity to the infection and on those biological species characteristics such as the area of distribution, census, nature of the colonies, the degree of contact with other individuals and species of mammals and particularly with ixodial ticks.

Mass species of animals of the first group, which constitute the main feeders of the larval and nymph phases of ixodial ticks (as well as the imagoes of certain species) account for the extensive spread of the pathogen in the foci and the transmission of bacteria by arthropod vectors. Extensive epizootics are well known among common voles, water rats, steppe lemmings, and house mice. A small number of animals in the first group and species in the second group are involved in the epizootic by virtue of their contact with the infected population, and with vectors and play a secondary part in the circulation of the pathogen.

The decline and extinction of the epizootic among highly sensitive animals are accomplished by a change in the ecological situation and a reduction in the intensity of contact between the animals, as a result of a reduction in their censuses, a seasonal change in the mode of life, a change in the structure of the colonies, etc. Of great importance is the seasonality of contact between the animals and the vectors. The influence of temperature conditions is of tremendous significance in the duration of the preservation of the pathogen in the bodies of the animals, in the environment as well as in the vectors.

Field epizootological investigations have established the existence of elementary foci of tularemia in definite landscape areas of endemic territory (Olsuf'yev, Kucheruk, 1955). The elementary foci possess stability, caused by the constant presence of ixodial ticks and the seasonal or constant abundance of warm-blooded hosts for the young stages of the tick. Under conditions of a river valley focus the elementary foci are located on the elevations in the terrain, which are not flooded during inundations and for this reason offer favorable conditions for the habitation of ixodial ticks and other ectoparasites and various species of small mammals. In the steppe foci the significance of elementary foci is acquired by depressions in the terrain covered with brush (gullies, ravines), by natural and artificial foresting, where a concentration of different species of mammals is observed (hamsters, voles) and where there are favorable conditions for the existence of ticks. Spread of the infection to adjacent territories occurs from the elementary foci when there are appropriate conditions, for example, with an increase in the censuses of the basic species here, seasonal migrations, etc. In the river valley type of focus extensive spread of the infection can occur as the result of passive migration of animals during a flood. The local character of elementary foci facilitates the task of sanitizing them.

Considerable work done by Soviet investigators has clarified the basic rules and regulations of tularemia epizootology in the Soviet Union. At the same time, a number of problems, which require further details, remain unclear. Through the example of study of specific epizootics it is necessary to elucidate successive pictures of the development of the epizootic process, the causes of occurrence and extinction of epizootics.

In various types of foci a more detailed study should be made of the means of circulation of the pathogen in specific elementary foci so that, by acting on various links of the epizootic chain, it might be possible to eradicate the focus.

Next in turn is the study of the existential conditions of tularemia in the north of the country, outside of the area of distribution of ixodial ticks, where low temperatures in the summer can contribute to prolonged preservation of bacteria in the gamasid ticks, and possibly in the environment also.

For specific conclusions about the epizootological significance of the most numerous animals of the second group in various foci detailed

experimental investigations and field epizootological investigations are necessary. There have been no adequate observations on the significance of tularemia epizootics in the regulation of the census of animals, particularly those necessary for trade (muskrat, hare).

Finally, study of the characteristics of the course of mixed infections, both experimentally and under natural conditions, is of considerable interest.

Conclusions

1. A characteristic feature of the study of tularemia epizootology in the USSR has been the comprehensive work of bacteriologists, zoologists and parasitologists, who have conducted field observations as well as experimental research.

2. Study of the biological properties of strains of Bacterium tularense isolated in different natural foci from various animals and environmental objects has shown that focal or epidemic strains circulate in nature which possess a high degree of virulence and which to a great degree are similar in different strains.

3. It has been confirmed by experimental investigations that with natural lines of circulation of the pathogen (passages through animals, preservation in ticks or in the environment) the virulence of the strains is not reduced.

4. Of primary significance in the formation and preservation of virulent properties of the tularemia microbe is the mechanism of transmission, which is accomplished in nature chiefly through blood-sucking arthropods, for the infection of which active seeding of the blood of the animals is necessary.

5. Spontaneous infection with tularemia has been recorded in 43 species of wild mammals in the USSR, but active epizootics are observed only in some species (water rat, common vole, house mouse, steppe lemming).

6. On the basis of an experimental study of the characteristics of the course of tularemia in wild animals (rodents, insectivores and carnivores) three types of relations of the animals to infection have been distinguished which determine the epizootological significance of the latter.

7. Through field observations in combination with experimental investigations it has been shown that the maintenance of natural foci of tularemia is accomplished by circulation of the pathogen among mass species of highly sensitive animals (first group), which provide for extensive spread of the infection over the territory and the infection of the ectoparasites.

8. The prolonged existence of natural tularemia foci is maintained chiefly by ixodial ticks; transmission of the tularemia pathogen can be accomplished also by some species of gamasid ticks (Hirstionyssus) and by lice. In the river valley type of focus mosquitoes are of more than a little importance in the spread of the infection.

9. The possibility of the chronic course of the infection in highly sensitive animals (water rats, voles and mice) has not been confirmed in experiments performed with highly virulent strains of the tularemia microbe. Post-infectious bacterial carriage in animals of the second group is of no epizootological significance, because the possibility of provocation of infection in the acute form is eliminated by the immunological reactions of the organism.

10. In the meadow-field and foothill-brook types of natural foci the existence of elementary tularemia foci has been demonstrated, which possess stability as the result of the constant presence here of ixodid ticks and constant or seasonal abundance of mammals-- the feeders of the ticks in the young stages.

11. A future problem in investigations on the epizootology of tularemia is the detailed study of lines of circulation of the pathogen in specific elementary foci so that, by acting on the various links of the epizootological chain, it might be possible to eradicate the focus.

pp 502-513

Percutaneous Vaccination against Brucellosis

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Preliminary Report

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Vaccine prophylaxis of brucellosis which is carried out in the Soviet Union by means of living brucellosis vaccine, the principles and methods of application of which in epidemiological practice have been worked out by P. A. Vershilova (1947, 1949), represents a considerable contribution to the work of preventing brucellosis in people. We shall not dwell here on the immunological and epidemiological effectiveness of the vaccine, because data on this subject have been generalized on by P. A. Vershilova and A. A. Golubeva (1956).

While vaccination against brucellosis, as is seen from this work, cannot be considered to have decisive significance in the matter of prophylaxis of this disease, still, according to the perfectly justified conclusion of P. F. Zdrodovskiy (1952) and V. M. Zhdanov (1954), it is, by virtue of the epidemiological characteristics of this infection, undoubtedly one of the main agents for protection of people against infection with brucellosis through direct contact with sources of infection in animal husbandry farms, where other measures against brucellosis, including a special routine of work in caring for animals sick with brucellosis, are not very effective. Herein lies the promise of specific vaccine prophylaxis of brucellosis which, however, by virtue of the immunity characteristics in this infectious disease, definitely needs an increase in its immunological and, therefore, epidemiological effectiveness. In addition, there is an urgent practical need for simplification of the method of vaccination itself as well as for the development of a revaccination method which, as is well known, "interferes" very much with residual immunological (particularly allergic) reactivity of the persons vaccinated.

Here, we shall not dwell on the subject of the number of times immunization should be carried out, which even with the use of living vaccines is of decisive importance in producing a postvaccinal immunity of high strength, which has been shown in anthrax by L. Pasteur (1884), L. S. Tsenkovskiy (1883-84), N. A. Mikhin (1942), in

plague by Ye. I. Korobkova (1956), and in tularemia by B. Ya. El'bert (1956). This problem has not been studied in brucellosis, although in this infectious disease, from our viewpoint, it deserves special attention for a number of reasons. For the purpose of reproducing a post-vaccinal immunity not only from the viewpoint of simplification of vaccination method but, chiefly, from the viewpoint of its results, the method of administering the vaccine is of more than a little importance. Thus, according to the data of A. M. Bezredka (1925) and N. A. Mikhin (1942), intradermal vaccination against anthrax is more effective than subcutaneous injection of the vaccine. Similar results have been obtained by Ye. I. Korobkova (1956) in the experimental study of vaccine prophylaxis of plague.

The immunological effectiveness of vaccine prophylaxis of brucellosis in experimental investigations on guinea pigs in accordance with the method of the injection of the vaccinal strains of living brucellas has been studied by P. A. Vershilova (1947, 1949, 1950) and by N. F. Zenkova (1956). Thus, according to the data of P. A. Vershilova, as the result of subcutaneous vaccination of 32 guinea pigs with a dose of 1,000,000,000 microbes of a vaccine strain of brucellas, "BA", all the guinea pigs were resistant not only to one but even to five infective doses of brucellas of the B. melitensis type after one month. At the same time, of 13 guinea pigs vaccinated intradermally with 250,000,000 microbes of the Brucella suis 22 strain, which is not pathogenic for these animals, only nine guinea pigs (69.2 percent) were resistant to five infective doses of brucellas of the B. melitensis type after the same interval of time. According to the data of N. F. Zenkova, all the guinea pigs, both vaccinated subcutaneously (eight animals) and percutaneously (six animals) not only with 1,000,000,000 but also with 500,000,000 microbes of the dry living brucellosis vaccine of the NIIEG [Scientific Research Institute of Epidemiology and Hygiene] were immune to one infective dose of brucellas of the B. melitensis type two months after vaccination. At the same time, in the experiment of P. A. Vershilova, only 18 animals (86.0 percent) out of 21 guinea pigs vaccinated subcutaneously with 1,000,000,000 microbes of a vaccine strain of brucellas, "BA", were found to be immune after the same interval of time to this infective dose of brucellas of the B. melitensis type.

From what has been stated it seems to follow that, according to the data of P. A. Vershilova, the immunological effectiveness of intradermal vaccination against brucellosis is less than that of subcutaneous vaccination, while according to the data of N. F. Zenkova, conversely, percutaneous vaccination is more effective than subcutaneous. However, as we shall see below, these data, which separately

are of considerable theoretical interest, are not comparable with one another.

First of all, in the experiments of P. A. Vershilova, a vaccine strain of "BA" brucellas was used for subcutaneous immunization which had been kept in the bodies of guinea pigs infected with 1,000,000,000 microbes from 20 to 40 days in 89 percent of the animals (in 16 out of 18 guinea pigs), and two months after the vaccination, in 50 percent of the animals (in 31 out of 61), whereas the B. suis strain used for intradermal vaccination, injected subcutaneously in a dose of 1,000,000,000 microbes, was no longer found on bacteriological examination on the 30th day in the majority of animals (Vershilova, 1947).

In addition, as P. A. Vershilova writes (1956), "For the purpose of creating strong immunity it is necessary to inoculate ... a dose of living brucellosis vaccine which would provide for a rapid seeding of the organism with the vaccine culture and an active immunological reorganization of the body, producing prolonged stimulation of the nervous and reticuloendothelial systems". In her experiments on guinea pigs this was achieved by means of subcutaneous inoculation of 1,000,000,000 microbes of brucellas of the "BA" strain, which had preserved residual virulence apparently to a much greater degree than the B. suis 22 strain, which, incidentally, had been injected into guinea pigs in a dose amounting to one-fourth of the dose of the "BA" strain of brucellas.

Secondly, P. A. Vershilova in her experiments made use of the "BA" vaccine strain, while N. F. Zenkova made use of the NIIEG vaccine strain. The degree of residual virulence, which plays the main part in immunogenesis, may be higher in the latter than in the "BA" vaccine strain, which, for example, occurs in the vaccine strain of brucellas, "M" (Zdrodovskiy, 1953).

In addition, the experiments of N. F. Zenkova are clearly inadequate for the conclusion of greater immunological effectiveness of percutaneous vaccination, because they were performed on a very small number of animals -- two-six guinea pigs.

From what has been stated it follows that postvaccinal immunity in brucellosis in guinea pigs can be reproduced not only by means of subcutaneous but also by means of intradermal and percutaneous vaccination. It is not possible to speak of an advantage of one method of vaccination over the others on the basis of the investigations of P. A. Vershilova and N. F. Zenkova. However, in this connection we should adhere to the opinion of N. F. Gamaleya, which he expressed on the immunogenesis in the skin. "Problems associated with skin immunity", writes N. F. Gamaleya, "should be studied in greater detail, because much in this field is still unknown, and at the present

time it is not being studied by anyone. This study will assist in clarifying many problems of immunity".

As far as the study of the sero-allergic reactivity of persons percutaneously vaccinated against brucellosis and the epidemiological effectiveness of this method of immunization are concerned, in this connection we know of only two works -- that of I. P. Druzhinina (in manuscript) and N. F. Zenkova (1956).

I. P. Druzhinina recorded the results of percutaneous vaccination (inner surface of the middle third of the forearm) conducted in Astrakhanskaya Oblast by workers of the NIIEG, who vaccinated not only those who showed a negative reaction for brucellosis but those who showed a positive reaction, including those who had been sick with the clinically overt form of this infectious disease. This, for entirely understandable reasons, somewhat complicates but does not rule out the possibility of drawing conclusions according to the results of study of this method of vaccine prophylaxis of brucellosis. The results of the study of the sero-allergic reactivity of those vaccinated are shown in Table 1.

From the data presented in this Table it is seen quite distinctly that percutaneous vaccination against brucellosis accounted for a marked increase in the sero-allergic reactivity of those vaccinated, whereby, as is characteristic of a vaccine-produced brucellosis, after subcutaneous injection of the vaccine (Vershilova, Feder and Polyakova, 1952), both by the Huddleson test and by the skin-allergic test of Burnet, it was most pronounced two-three and five months after vaccination (4.9 and 4.1 times greater than the original by the Huddleson test and 5.2 and 4.3 times greater by the Burnet test).

In Table 2 the comparative data of N. F. Zenkova (1956) are presented on the sero-allergic reactivity of those vaccinated percutaneously and subcutaneously with dry living brucellosis vaccine of the NIIEG in the KazSSR.

From the data presented in Table 2 it is seen that not only percutaneous but also subcutaneous immunization of people against brucellosis by means of living vaccine does not always cause an immunological reorganization of those vaccinated (12 percent by the serological reactivity and 44.3 percent by the allergic reactivity), whereby percutaneous vaccination was less immunogenic than subcutaneous (by 1.2-1.8 times). However, according to N. F. Zenkova, this did not have any negative effect on the epidemiological effectiveness of vaccination.

In the study of the epidemiological effectiveness of percutaneous vaccination against brucellosis positive results were obtained by both I. P. Druzhinina and N. F. Zenkova. Thus, according to the data of I. P. Druzhinina, in the "P" sheep-raising sovkhoz, which was af-

Table 1

Sero-Allergic Reactivity of Persons Percutaneously Vaccinated against Brucellosis (according to I. P. Druzhinina Manuscript, 1951)

Где проводилась вакцинация	Положительно реагировало (в процентах)									
	по реакции Хеддльсона					по кожной пробе Бюрнэ				
	до вакцинации	после вакцинации через:				до вакцинации	после вакцинации через:			
		2 мес.	5 мес.	13 мес.	19—20 мес.		3 мес.	5 мес.	13 мес.	19—20 мес.
Овцесовхоз „П"	15,8	92,5	90,3	31,4	33,1	13,4	73,3	[illegible]	59,0	47,0
Овцесовхоз „С"	26,1	83,9	90,0	—	—	16,6	[illegible]	85,7	—	—
Мясомолочный совхоз „А"	22,1	85,1	66,6	—	15,5	11,6	87,3	78,0	—	39,1
Колхоз „У"	7,4	84,6	52,4	—	—	6,7	70,6	76,0	—	—
Пос. Приволжье	11,7	90,9	76,2	87,5	63,7	5,5	71,4	50,0	72,7	75,0
В среднем	17,9	88,4	74,3	43,1	32,0	14,2	[illegible]	61,3	53,4	47,6
Во сколько раз выше исходного	—	4,9	4,1	2,4	1,6	—	5,2	4,3	3,7	3,3

1. Where vaccination was conducted; 2. Those reacting positively (in %); 3. By the Huddleson test; 4. Before vaccination; 5. Time after vaccination: 6. Months; 7. By the Burnet skin test; 8. Before vaccination; 9. Time after vaccination: 10. The "P" sheep-raising sovkhoz; 11. The "S" sheep-raising sovkhoz; 12. The "A" meat and dairy sovkhoz; 13. The "U" kolkhoz; 14. Privolzh'ye settlement; 15. On the average; 16. Number of times greater than the original.

fected more by brucellosis than all the other foci used by the author together, one year after vaccination six patients with brucellosis were found, including one vaccinated and five nonvaccinated persons, and two years after vaccination 21 persons became sick with brucellosis; of these six had been vaccinated and 15 had not been vaccinated.

In a comparative study of the epidemiological effectiveness of percutaneous and subcutaneous vaccination against brucellosis N. F. Zenkova determined the fact that six months after vaccination in various foci of infection among those vaccinated percutaneously from 0 to 0.8 percent became sick with brucellosis (on the average, 0.28 percent), while among those vaccinated subcutaneously this figure was from 0.7 to 0.8 percent; a year after vaccination 0.5 percent (10 per-

Table 2

Comparative Sero-Allergic Reactivity of Persons Percutaneously and Subcutaneously Vaccinated against Brucellosis (after Zenkova, 1956)

(1) Способ вакцинации	(2) Положительно реагировало (в процентах) после вакцинации											
	(3) по реакции Райта через						(4) по кожной пробе Бюрне через					
	1 мес. (5)	3 мес. (5)	6 мес. (5)	12 мес. (5)	24 мес. (5)	36 мес. (5)	1 мес. (5)	3 мес. (5)	6 мес. (5)	12 мес. (5)	24 мес. (5)	36 мес. (5)
(6) Накожно	79,6	61,4	60,5	35,9	66,6	42,6	46,6	23,4	39,7	34,4	58,6	51,0
(7) Подкожно	—	76,1	83,0	67,3	—	52,1	—	45,7	50,0	55,7	—	60,0
(8) Во сколько раз выше, чем накожно	—	1,2	1,4	1,8	—	1,2	—	1,2	1,2	1,6	--	—

1. Method of vaccination; 2. Those reacting positively (in %) after vaccination; 3. By the Wright test after: 4. By the Burnet skin test after: 5. Months; 6. Percutaneously; 7. Subcutaneously; 8. No. of times greater than percutaneous method.

sons) became sick among those vaccinated percutaneously, and 1.3 percent (15 persons) among those vaccinated subcutaneously. From what has been stated it follows that percutaneous vaccination against brucellosis was epidemiologically 2.6 times more effective than subcutaneous vaccination.

Not only the lower brucellosis morbidity rate among those vaccinated than the morbidity among those not vaccinated is evidence of the epidemiological effectiveness of percutaneous vaccination (according to the data of N. F. Zenkova, in various foci of infection it is from four to seven and even 11 times more effective), but the increased sero-allergic reactivity of those vaccinated after a second chance of becoming infected with brucellosis also attests to this.

As is seen from Table 2, the serologic and allergic reactivity of those vaccinated percutaneously increased again by 1.8 times by the Wright test (in 66.6 percent of the vaccinated as against 35.9 percent) and by 1.7 times by the Burnet test (in 58.6 percent of those vaccinated as against 34.4 percent), following a natural reduction of it toward the end of the first year after vaccination, after the next year in the midst of complete health of those vaccinated. This, according to

the opinion of P. F. Zdrodovskiy (1953) is evidence of contact bet... en those vaccinated and sources of brucellosis which did not cause the dis-ease but rather a natural "revaccination".

A similar phenomenon was noted by I. P. Druzhinina with respect to part of the workers of the "P" sheep-raising sovkhoz, who prior to subcutaneous vaccination had reacted negatively for brucellosis and who by the nature of their work activity had opportunities of becoming infected from sheep sick with brucellosis but who were healthy 13 and 19-20 months after vaccination (see Table 3).

Table 3

Sero-Allergic Reactivity of Workers in the "P" Sheep-Raising Sovkhoz Vaccinated Percutaneously against Brucellosis Who Had Shown Negative Reactions for Brucellosis Prior to Vaccination (after I. P. Druzhinina, Manuscript 1951)

Категории вакцинированных	По реакции Хеддльсона после вакцинации через:				По пробе Бюрнэ после вакцинации через:			
	13 мес.		19-20 мес.		13 мес.		19-20 мес.	
	обследовано	из них реагировало положительно	обследовано	из них реагировало положительно	обследовано	из них реагировало положительно	обследовано	из них реагировало положительно
Имевшие возможность инфицироваться . .	28	11	34	16	23	15	35	21
Не имевшие возможности инфицироваться	6	0	7	1	6	2	7	3

1. Categories of persons vaccinated; 2. By the Huddleson test according to months after vaccination; 3. By the Burnet test according to months after vaccination; 4. Months; 5. Investigated; 6. Of these the number who reacted positively; 7. Those who had a chance to become infected; 8. Those who did not have an opportunity of becoming infected.

These are the results of the analysis of data in the literature at our disposal on percutaneous vaccination against brucellosis.

Our investigations were along two lines. On the one hand, G. A. Balandin, I. I. Polyakov, N. P. Prostetova and L. I. Korobov

in experiments on guinea pigs made a study of the comparative immunological effectiveness of percutaneous and subcutaneous vaccinations of these animals with a vaccine strain of brucellas, "BA" (B. abortus 19 strain) and, on the other hand, under the direction of G. A. Balandin in Krasnodarskiy Kray (Ye. M. Kral'), in Rostovskaya (O. Yu. Reznikova, N. A. Chernenkova and N. D. Bobyreva) and Stalingradskaya oblasts (E. G. Tomberg and N. A. Lisitsyna) a study was made of the sero-allergic reactivity of persons percutaneously vaccinated and revaccinated with living brucellosis vaccine of the IEM [Institute of Epidemiology and Microbiology] of the Academy of Medical Sciences USSR and the epidemiological effectiveness of this method of prophylaxis of brucellosis.

Although our experimental investigations at the time of writing this article have not been completed, we can still present some data on the comparative development of vaccine brucellosis in guinea pigs vaccinated (resp. infected) subcutaneously and percutaneously with different doses of brucellas of the "BA" strain as well as certain comparative data on the immunogenic properties of this strain of brucellas depending on the method of vaccination of the animals.

The characteristics of development of vaccine brucellosis depending on the method of infection of the guinea pigs were studied by means of bacteriological examination of these animals, infected subcutaneously and percutaneously with a two-day agar culture of brucellas of the "BA" strain in doses of 1,000, 10,000, 1,000,000, 1,000,000,000 and 10,000,000,000 microbes five, 15, 30 and 45 days after infection. In each experimental group of animals there were five-10 guinea pigs. The results of the investigations are presented in Table 4.

Without going into a detailed analysis of the data obtained we should like to note only that generalized vaccine infection in guinea pigs, without which postvaccinal immunity against brucellosis of sufficiently high strength cannot develop, in P. A. Vershilova's opinion (1956), is produced either by subcutaneous injection of 1,000,000,000 microbes of the vaccine strain of "BA" brucellas or by percutaneous application of 10,000,000,000 microbes of the same strain of brucellas.

In addition, from Table 4 it is seen that subcutaneous injection of brucellas produces a relatively slow and then more prolonged development of brucellosis vaccine infection, whereas percutaneous application of brucellas produces a rapid (as early as after five days) development of generalized vaccine infection and a rapid (by the 45th day) complete elimination of the pathogen of the vaccine infectious process from the bodies of guinea pigs. What has been stated is to some degree in accordance with the statement presented above by N. F. Gamaleya concerning the role of the skin in immunogenesis, which, as is seen

Table 4

Characteristics of Development of Vaccine Brucellosis in Guinea Pigs in Accordance with the Method of Infection of Them with a Vaccine Strain of Brucellas, "BA"

Заражающая доза (число микробных тел) (1)	Метод заражения (2)	(3) Число животных с разной степенью развития инфекции через																			
		5					15					30					45 дней (9)				
		Всего (4)	стерильные (5)	с регионарной инфекцией (6)	с генерализованной инфекцией (7)	с локализованной инфекцией (8)	Всего (4)	стерильные (5)	с регионарной инфекцией (6)	с генерализованной инфекцией (7)	с локализованной инфекцией (8)	Всего (4)	стерильные (5)	с регионарной инфекцией (6)	с генерализованной инфекцией (7)	с локализованной инфекцией (8)	Всего (4)	стерильные (5)	с регионарной инфекцией (6)	с генерализованной инфекцией (7)	с локализованной инфекцией (8)
1 тыс. (12)	(10) подкожно	5	5	—	—	—	5	3	2	—	—	5	4	1	—	—	5	4	1	—	—
	(11) накожно	5	5	—	—	—	5	4	1	—	—	5	5	—	—	—	5	4	1	—	—
100 тыс. (12)	(10) подкожно	5	1	4	—	—	5	3	2	—	—	5	1	2	2	—	5	2	1	—	2
	(11) накожно	5	3	[illegible]	—	—	5	0	5	—	—	5	3	2	—	—	5	4	1	—	—
1 млн. (13)	(10) подкожно	5	—	4	1	—	5	—	3	2	—	5	3	1	1	—	5	1	3	1	—
	(11) накожно	5	2	3	—	—	5	1	4	—	—	5	—	4	1	—	5	3	1	1	—
1 млрд. (14)	(10) подкожно	10	—	2	8	—	10	—	2	8	—	10	—	5	5	—	5	—	1	3	1
	(11) накожно	5	—	5	—	—	5	—	4	1	—	5	1	2	2	—	5	—	3	1	1
10 млрд. (15)	(11) накожно	5	—	—	5	—	5	—	2	3	—	4	—	1	1	2	5	5	—	—	—

1. Infective dose (no. of microbes); 2. Method of infection; 3. No. of [illegible] with different degrees of development of the infection after: 4. Total; 5. Sterile; 6. With regional [illegible]; 7. With [illegible]; 8. With localized infection; 9. Days; 10. Subcutaneously; 11. [illegible]taneously; 12. Thousand (s); 13. Million; 14. Billion; 15. Billions.

from Table 5, has a quite distinct influence on the development of immunity to brucellosis with respect to the resistance of percutaneously vaccinated guinea pigs to superinfection with brucellas of the B. melitensis type.

Table 5

Comparative Resistance of Guinea Pigs Vaccinated Subcutaneously and Percutaneously with Brucellas of the B. abortus type ("BA" Vaccine Strain) to Superinfection with Brucellas of the B. Melitensis type in a Dose of 10 Microbes

(1) Срок суперинфекции после вакцинации (дни)	(2) Вакцинированные подкожно 1 млрд м. т.				(3) Вакцинированные накожно 10 млрд м. т.			
	(4) количество животных	(5) из них: заразилось Br. melitensis (6)	(5) из них: имели Br. abortus (7) (инфекцион. иммунитет)	(8) Наличие иммунитета (условно в %)	(4) количество животных	(5) из них: (6) заразилось Br. melitensis	(5) из них: (7) имели Br. abortus (инфекцион. иммунитет)	(8) Наличие иммунитета (условно в %)
1	10	10	0	0	10	9	1	10,0
3	10	9	1	10,0	10	8	2	20,0
5	10	9	1	10,0	10	6	4	40,0
(9) Контроль	15	15	0	0	9	9	0	0

1. Time of superinfection after vaccination (days); 2. Vaccinated subcutaneously with 1,000,000,000 microbes; 3. Vaccinated percutaneously with 10,000,000,000 microbes; 4. No. of animals; 5. Of these, the number; 6. Infected with B. melitensis; 7. Which had B. abortus (infectious immunity); 8. Presence of immunity (arbitrarily, in %); 9. Control.

From the data presented in Table 5 it is seen that percutaneous vaccination of guinea pigs with 10,000,000,000 microbes of a vaccine strain of "BA" brucellas was responsible, as early as three-five days after vaccination, for a resistance to superinfection with 10 microbes of the B. melitensis type of brucellas (in our investigations, five infective doses) which was two to four times greater than subcutaneous immunization of these animals with 1,000,000,000 microbes of the same vaccine strain of brucellas.

It was also determined that guinea pigs vaccinated percutaneously gave negative sero-allergic reactions for brucellosis one, three

and five days after vaccination. Guinea pigs vaccinated subcutaneousl reacted positively in the Huddleson test and by the Wright test five days after vaccination (with an average agglutination titer of 1:50), with negative brucellin reactions in the Burnet test and with a normal phagocytic activity of leukocytes for animals not infected with brucellosis (index, from 2 to 5). Therefore, in this case the sero-allergic reorganization of the vaccinated (resp. infected) organism, which in P. A. Vershilova's (1956) opinion is essential, was of no significance in this case for the development of the infectious immunity to brucellosis. In this case apparently the rapid (as early as on the day after vaccination) and active seeding of the vaccinated organism (generalized infection) with brucellas, which was achieved by the application of a dose of a vaccine strain of brucellas which was 10 times that of the dose of brucellas used for subcutaneous vaccination to the scarified skin of the guinea pigs, was of decisive importance in immunogenesis.

Let us proceed with a presentation of the results of study of the sero-allergic reactivity of persons vaccinated and revaccinated percutaneously with living brucellosis vaccine of the IEM of the Academy of Medical Sciences USSR and the epidemiological effectiveness of this method of vaccination against brucellosis.

For the purpose of giving the inoculations a series of dry living brucellosis vaccine which contained 1,000,000,000 microbes per drop in a single inoculation dose (after dilution of it with physiological saline solution) was used which had been prepared specially for this purpose by the Institute of Epidemiology and Microbiology of the Academy of Medical Sciences USSR. In parallel with this subcutaneous vaccination was carried out in a number of foci of brucellosis by means of the same series of vaccine which, however, contained the usual number of microbes which are utilized in vaccine prophylaxis of brucellosis at large in a single inoculation dose.

Vaccination (subcutaneous and percutaneous) and revaccination (percutaneous only) were carried out in the sheep-raising sovkhozes and kolkhozes which were unfavorable with respect to brucellosis of short-horned cattle, and in meat combines which slaughtered cattle sick with brucellosis.

All persons being inoculated against brucellosis were first investigated for brucellosis by means of the Huddleson and Burnet tests. Only those showing negative reactions were vaccinated, while all those previously vaccinated were revaccinated regardless of their sero-allergic reactivity for brucellosis.

The side-effects produced by percutaneous vaccination and the reactivity of those being revaccinated percutaneously was so slight that it was practically unnoticed by the persons being inoculated them-

selves and those giving the inoculations. The sero-allergic reactivity of those vaccinated and revaccinated was studied by the Huddleson and Burnet tests at three periods: 50-150 days; 151-300 days and 301-450 days after vaccination and revaccination. The results of these investigations are shown in Tables 6 and 7.

Table 6

Postvaccinal Sero-Allergic Reactivity of People at Various Intervals after Percutaneous and Subcutaneous Vaccination of Them with Dry Living Brucellosis Vaccine of the IEM of the Academy of Medical Sciences USSR

Сроки после вакцинации в днях	Всего обследовано	Из них реагировали: X − и Б − в абс. цифрах	в %	X + и Б − в абс. цифрах	в %	X + и Б + в абс. цифрах	в %	X − и Б + в абс. цифрах	в %	Всего реагировало положительно (в %) серологически (X)	аллергически (Б)
Вакцинированные накожно											
50—150	121	61	50,4	18	14,9	18	14.9	24	19,8	29,8	34,7
151—300	49	19	33,3	17	34,7	4	8,2	9	18,3	42,9	26,5
301—450	47	23	59,6	8	17,0	8	17,0	3	6,4	34,0	23,4
Вакцинированные подкожно											
50—150	34	8	23,5	11	32,3	9	26,5	6	17,7	58,8	41,2
151—300	44	9	20,4	11	25,0	18	40.9	6	13,7	65,9	54,6
301—450	150	51	34,0	15	10,0	38	25,3	46	30,7	35,3	56,0

Key: (X) -- Huddleson test; (B) -- Burnet test; (+) -- positive test; (-) -- negative test. 1. Time after vaccination in days; 2. Total persons examined; 3. Of these, the number which reacted: 4. In absolute numbers; 5. In %; 6. Total which showed a positive reaction (in %); 7. Serologically (X); 8. Allergically (B). 9. Vaccinated percutaneously; 10. Vaccinated subcutaneously.

From Table 6 it is seen that as the result of percutaneous application of living brucellosis vaccine, even in a dose of 1,000,000,000 microbes, neither serological nor allergic reorganization was noted 50-150 days after vaccination in 50.4 percent of those vaccinated, whereas in those vaccinated subcutaneously the negative result after this period of time was shown only by 23.5 percent of those vaccinated that is, 2.1 times less. Passing over, for the moment, data on the

Table 7

Postvaccinal Sero-Allergic Reactivity of People at Various Intervals after Percutaneous Revaccination with Dry Living Brucellosis Vaccine of the IEM of the Academy of Medical Sciences USSR

(1) Реакция до ревакцинации	(2) Сроки после ревакцинации в днях	(3) Всего обследовано	(4) Реагировало после ревакцинации				(5) Всего реагировало положительно (условно в %)	
			X−Б−	X+Б−	X+Б+	X−Б+	(6) серологически (X)	(7) аллергически (Б)
X−B−	50−150	30	13	7	7	7	[illegible],0	36,0
•	151−300	33	16	12	8	2	52,6	26,3
•	301−450	45	21	5	11	8	35,5	42,9
X+B−	50−150	15	5	6	3	1	60,0	26,6
•	151−300	27	6	8	8	5	59,3	48,1
•	301−450	53	11	22	11	9	62,3	37,7
X+D+	50−150	7	1	1	4	1	71,4	71,4
•	151−300	13	-	3	5	5	61,5	77,0
•	301−450	8	3	—	5		62,5	62,5
X−B+	50−150	23	7	2	4	10	26,1	60,9
•	151−300	15	6	—	2	7	13,3	60,0
•	301−450	14	2	—	6	6	42,8	35,7

Key is the same as for Table 6.

1. Reaction before revaccination; 2. Time after revaccination in days; 3. Total persons examined; 4. No. which reacted after revaccination; 5. Total reacting positively (arbitrarily, in %); 6. Serologically (X); 7. Allergically (B).

serological reactivity of those vaccinated 151-300 days after vaccination, we consider it necessary to note that allergic reactivity of the skin (positive results with the Burnet test) after percutaneous vaccination developed within the limits of our observation period (450 days) in a diametrically opposite direction from the development of the allergic state in those vaccinated subcutaneously. After percutaneous vaccination it gradually but steadily decreased, whereas after subcutaneous vaccination this condition gradually increased.

From what has been stated it follows that vaccine brucellosis produced by subcutaneous injection of living brucellas follows the rules and regulations of development of this reactivity in a natural brucellosis infection in its allergic representation. A vaccinal infection produced

by percutaneous application of brucellas is a somewhat distinctive infectious process, in which the specific allergization of the vaccinated organism develops not only in a smaller number of those vaccinated (34.7 percent as against 44.2 percent) but also in a shorter period of time than after subcutaneous vaccination. This unique phenomenon occurs against the background of almost equal serological reactivity in those vaccinated subcutaneously (35.3 percent) and those vaccinated percutaneously (34.0 percent).

This very interesting phenomenon, noted specifically in a group of persons revaccinated percutaneously who prior to revaccination had reacted negatively for brucellosis (see Table 7), which we determined, unfortunately, on a small quantity of material, requires further study. First of all, it will possibly enable us to clarify certain features in the mechanism of development of immunity in the skin and, secondly, will make it easier for us to differentiate sero-allergic reactions for brucellosis in persons naturally infected with brucellosis and people percutaneously vaccinated against this infectious disease.

As far as persons are concerned who were revaccinated with living brucellosis vaccine, those of them who prior to revaccination reacted positively in the Huddleson test preserved this serological reactivity for a longer period than those who showed a negative reaction (see Table 7). The same thing was noted with respect to the allergic reactivity of those revaccinated who had reacted positively in the Burnet skin test before revaccination. However, these changes in the sero-allergic reactivity in the direction of a recovery of it, preservation or intensification in it were not observed in a considerable number of those revaccinated not only in the remote (30.5 percent) but also in the immediate periods (37.0 percent) after revaccination. Therefore, percutaneous revaccination against brucellosis, despite the additional antigenic stimulation by nonpathogenic brucellas of the vaccine strain, by far does not always cause the appearance of positive changes in the serological and allergic reactivity of those revaccinated, attesting to "recovery" of lost or declining postvaccinal immunity to brucellosis.

With respect to changes in the serological reactivity of persons vaccinated percutaneously and subcutaneously who had reacted negatively for brucellosis prior to revaccination and who did almost exactly the same after revaccination, more will be said below.

The epidemiological effectiveness of percutaneous vaccination and revaccination against brucellosis was recorded only in those foci of the infectious disease where those being vaccinated were actually threatened with the possibility of infection with brucellosis -- in animal husbandry farms by aborting sheep and at the meat combines by short-horned cattle sick with brucellosis slaughtered for meat. The results of this record are shown in Table 8.

Table 8

Result of Record of Epidemiological Effectiveness of Percutaneous Vaccination and Revaccination against Brucellosis

1 Очаги бруцеллезной инфекции	10 Обследовано перед вакцинацией и ревакцинацией: 11 первично: 13 всего	первично: 14 из них дали реакцию на бруцеллез: 15 положительную	первично: из них дали реакцию на бруцеллез: 16 отрицательную	12 вакцинированных: 13 всего	вакцинированных: 14 из них дали реакцию на бруцеллез: 15 положительную	вакцинированных: из них дали реакцию на бруцеллез: 16 отрицательную	17 Вакцинировано: 18 подкожно	Вакцинировано: накожно	Ревакцинировано накожно	Не вакцинировано	Заболели бруцеллезом: вакцинированные подкожно	Заболели бруцеллезом: вакцинированные накожно	Заболели бруцеллезом: ревакцинированные	Заболели бруцеллезом: невакцинированные
2 Овцесовхоз „П"	262	205	57	52	19	33	—	26	52	31	—	—	—	1
3 Овцесовхоз им. Ю-на	34	—	34	21	17	4	18	16	21	—	1	—	1	—*
4 Колхоз им. Ленина	—	—	—	29	3	26	—	—	29	—	—	—	1	—
5 Кр. мясокомбинат	136	97	39	289	20	269	58	188	43	39	1	—	—	—
6 Нов. мясокомбинат	61	46	15	43	32	11	12	—	33	3	1	—	—	—
7 Рост. мясокомбинат	30	1	29	29	14	15	14	16	29	—	1	—	—	—
8 Всего: в абс. цифрах	523	319	174	463	105	358	102	246	203	73	4	—	2	1
9 в %		66,7	33,3		22,6	77,4					3,9	—	1,0	1,4

Note. In the sovkhoz im. Yu-n one person from the group of unvaccinated [illegible] taken on the record became sick with brucellosis (noted with an *).

1. Foci of brucellosis; 2. "P" sheep-raising sovkhoz; 3. Sheep-raising sovkhoz im. Yu-n; 4. Kolkhoz im. Lenin; 5. Kr. meat combine; 6. Nov. meat combine; 7. Rost. meat combine; 8. Total: in absolute numbers; 9. In %; 10. Investigated before vaccination and revaccination; 11. Originally; 12. Vaccinated; 13. Total; 14. Of these, the number which gave the following kinds of reactions for brucellosis; 15. Positive; 16. Negative; 17. Vaccinated; 18. Subcutaneously;

[Legend continued next page]

[Legend continued from previous page]. 19. Percutaneously; 20. Revaccinated percutaneously; 21. Not vaccinated; 22. Became sick with brucellosis; 23. Vaccinated subcutaneously; 24. Vaccinated percutaneously; 25. Revaccinated; 26. Not vaccinated.

From this Table it is seen that among those vaccinated subcutaneously 3.9 percent became sick with brucellosis; among those revaccinated, 1.0 percent; among those not vaccinated, 1.4 percent, whereas among those vaccinated percutaneously no cases of brucellosis were found in any of these foci of infection.

Evidence of the epidemiological effectiveness of percutaneous vaccination is afforded not only by the absence of cases among those vaccinated percutaneously but also by the increase in the number of people vaccinated and revaccinated percutaneously who reacted positively in the Huddleson test 151-300 days after inoculations (Tables 6 and 7). This with good reason can be considered the result of infection of those vaccinated and revaccinated with highly pathogenic brucellas of the goat-sheep type, wherein the brucellas penetrating into their bodies played the part of a revaccinating rather than infecting factor. The same was observed with respect to serological reactivity in the Huddleson test in those vaccinated subcutaneously. Similar phenomena, as has been mentioned above, were noted not only in those vaccinated percutaneously (Druzhinina and Zenkova) but also in those vaccinated subcutaneously (Rozova, Chernenkova, Reznikova, Bobyreva, Kireyeva, 1954; Pavlova, Sergeyeva and Martirosov, 1955; Zenkova, 1956).

Our investigations on the immunological and epidemiological effectiveness of percutaneous vaccination against brucellosis are not yet complete. However, considering everything presented here, we consider the percutaneous method of vaccinating people against brucellosis promising and requiring further study both experimentally and in epidemiological practice.

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Study of the Natural Focalization of Human Disease in its Application to the Regional Characteristics of Kazakhstan

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Study of the natural focalization of diseases, the founder of which is Academician Ye. N. Pavlovskiy, is entirely applicable to the practical problems not only of public health but also of animal husbandry. It has been extensively represented in the development of the theoretical basis of biology and in the practical activity of medical and veterinary institutions and it rightfully occupies its proper place among a number of major national economic problems of medical, veterinary and general biological significance.

The phenomenon of natural focalization of diseases is most closely associated with the geographic conditions of the locality, with the entire combination of natural-historical circumstances. In this respect, Kazakhstan is exceptionally convenient, if we may express ourselves in this way, for the investigator. The territory of Kazakhstan is quite large. It is five times larger than the area of France; three-four times the area of the Ukraine, and constitutes about a fourth of the area of the RSFSR.

The natural-geographic characteristics of Kazakhstan, which includes the main area of steppes, semideserts and deserts of the Southeast of the Soviet Union, which are bordered on the South and Southeast by mountain ranges, are characterized by a great variety of landscapes. Along with the areas of steppes and different variants of deserts with all the characteristics of climate, soil, vegetation and animals inherent in them, within the limits of Kazakhstan clearly expressed areas of taiga and forest steppe and, finally, large mountain ranges may be seen with a well developed vertical zonality.

In accordance with the variety of landscape-geographic circumstances the animal world of Kazakhstan is rich and varied, and the species composition of parasitic arthropods is particularly numerous. Here, along with the taiga forms of blood-sucking insects there are combinations of desert species of ectoparasites. The biocenoses of burrow holes are particularly rich in parasitic arthropods. Ixodial, argasid, gamasid ticks and thrombiculid mites, gnats, fleas, lice, black-flies and mosquitoes are the usual inhabitants of the burrow holes of steppe, desert and semidesert landscapes of Kazakhstan.

The landscapes of mountains, forest steppe, and numerous bottom lands of inland water bodies are rich in forest steppe and taiga species of ixodial ticks; the vermin in various biotopes of these landscapes is abundant and consists of diverse components. The characteristics of the landscape-geographic circumstances, the richness and variety of the

animal world inhabiting Kazakhstan are the natural basis for extensive development of human and agricultural animal diseases here with the phenomenon of natural focalization. I daresay, there are few natural focal diseases characteristic of Eurasia which are not known in Kazakhstan or which might not be expected within its limits. Along with such a taiga form as tick-borne encephalitis is, forms unknown in Kazakhstan which are characteristic of the deserts in the South of the country, for example, tick-borne relapsing fever, leishmaniases, pappataci fever and others. In the present report we shall dwell on the analysis of the main diseases with natural foci represented within the boundaries of Kazakhstan, the study of which has been made by groups of the Academy of Sciences of the KazSSR.

Natural foci of tick-borne encephalitis are found in a number of places in Kazakhstan. The area of distribution of this disease is a continuation of the known foci of this infectious disease in West Siberia and in the Altay. It extends throughout the entire forest strip of the mountain landscape of the Republic. In the forest strip of Zayliyskiy Ala-Tau, in the immediate vicinity of the city of Alma-Ata, lies the Alma-Ata focus of tick-borne encephalitis which is already well known in the literature. The reservoirs of the virus of tick-borne encephalitis here have been found to be inhabitants of mountain landscapes--the Altay marmot (Marmota baibacina) and the small-head voles (Stenocranius gregalis). Ticks (Ixodes persulcatus and Haemaphysalis punctata) have been found to be the vectors.

A second distinctly expressed focus of tick-borne encephalitis in Kazakhstan, according to the research data of the Republic Sanitary-Epidemiological Station (Dr. S. I. Rybalko and others) is in Vostochno-Kazakhstanskaya Oblast in the region of the Ust'-Kamenogorsk-Zyryanovsk railroad. This focus lies on the northern slopes of mountains covered with mixed forest. The reservoirsof the virus in this focus, according to the data of Professor Zhumatov, corresponding member of the Academy of Sciences of KazSSR, are I. persulcatus ticks.

Sporadic cases of tick-borne encephalitis also occur in the steppe and forest steppe regions of the Republic. Various cases have been recorded in Semipalatinskaya, Kokchetavskaya, Kustanayskaya and Karagandinskaya Oblasts. In these areas I. persulcatus ticks are absent, and Professor Zhumatov has not yet isolated the virus from the very common Dermacentor marginatus ticks present here.

The structure of the natural foci of tularemia lying within the boundaries of Kazakhstan have their own characteristic features. In many places of the Republic, together with types of foci characteristic of the central oblasts of the European part of the Soviet Union (meadow-field, alluvial plain and forest), there are, as has been determined by our former colleague V. P. Bozhenko, natural foci of the mountain-valley type which produce outbreaks of tularemia which are mainly of water origin. In this type of focus, according to the same data, new links are coming out in the cycle of the tularemia pathogens in nature --toads, mollusks, fish, and leeches.

In the Western Zone of KazSSR D. A. Golov, A. N. Knyazevskiy and V. M. Tumanskiy observed tularemia outbreaks among rodents beginning with 1929, and V. M. Tumanskiy in 1936 described tularemia epizootics observed here in dwarf sousliks (Citellus pygmaeus). After Tumanskiy, such phenomena were not seen by anyone for a long time there. However, we know from the report of P. N. Kucherov and co-authors (1957) of a tularemia epizootic in West Kazakhstan which occurred in 1952-1955, at which time sousliks were involved in the epizootic along with the steppe lemming (Lagurus lagurus). One of us (M. R.) isolated the tularemia pathogens in an endemic focus from the bodies of intermediate sousliks (Citellus intermedius) caught in a desert region.

In connection with this, we should not overlook the data of N.F. Kolacheva, P. I. Kamnev and A. D. Luk'yanova (1957), who isolated tularemia cultures from hares and Rhipicephalus pumilio ticks in the lowlands of the Chu River. All this is evidence of the presence of steppe and soddy-alluvial-desert foci of tularemia, aside from the types of natural foci known previously, in which the souslik, hare, steppe lemming and the desert ticks, Rh. pumilio and Rh. schulzei are the main objects in the disease and vectors of the infection.

In other landscape zones of Kazakhstan muskrats which live in the majority of fresh water bodies of the Republic and occupy a leading place in the fur industry here are involved in the cycle of the tularemia pathogen. According to the observations of our co-worker Ye. I. Strautman (1957), in water bodies where the muskrat is encountered along with the water vole (Arvicola terrestris) not uncommonly tularemia epizootics occur among muskrat populations. The cases first appear among water voles and only later are the muskrats involved in the epizootic. In those places where there are no water voles cases of tularemia are unknown among muskrats, and, conversely, mass multiplication of water voles is accompanied by a very active tularemia epizootic among muskrats over considerable territories, which leads to a marked reduction in the census of these rodents.

Tularemia epizootics among muskrats are accompanied by cases among hunters and other persons dealing with rodents.

The problem of tick-borne relapsing fever -- its vectors, focalization and distribution in Kazakhstan is not only of regional but also of general interest as an index of the natural geographic conditions under which the existence of natural foci of this infection is possible when it advances to the North.

The investigations of one of us (I. G.) showed that the northern boundary of the area of distribution of vectors of this infection -- the ticks Ornithodorus papillipes and O. tartakovskyi -- extend to 45° north latitude. The habitat of O. tartakovskyi ticks is associated with a desert and semidesert landscape. Living literally next to O. papillipes, these ticks are never encountered together with them, just as they are never encountered in the outbuildings or houses of man.

In places which O. papillipes ticks live one of us (I. G.) produced infection of a number of experimental laboratory-and-wild-animals

with tick-borne relapsing fever. Here, a man was also infected (our co-worker). From the ticks collected here a strain of spirochetes was isolated which has been maintained in our laboratory and given to the laboratory of Academician Ye. N. Pavlovskiy.

In colonies of great sand rats (Rhombomys opimus) which are infested with O. tartakovskyi ticks, infection of people has also occurred (our co-workers). From O. tartakovskyi ticks collected in this area we (N. G.) also isolated strains of spirochetes. More than 30 species of mammals inhabit the areas in which O. papillipes and O. tartakovskyi ticks live. All of them, to one degree or another, are in contact with the habitats of O. papillipes and O. tartakovskyi ticks and are their temporary or permanent hosts.

Of special interest are the animals on which these species of ticks feed alternately. Among them are: the long-eared hedgehog, Mongolian pika /Ochotona daurica/, gray hamster, mottled polecat /Vormela peregusna/, Siberian polecat, weasel, wolf, fox, Tartar fox, Egyptian cat /Felis lybica/, Central Asian gazelle, and Central Asian sheep /Ovis polii/. The investigation of the blood of wild animals in the area of distribution of the ticks O. papillipes and O. tartakovskyi made it possible for one of us (N.G.) to determine the existence of spirochetes in the great sand rat, Central Asian gazelle (Gazella subgutturosa), sand hare (Lepus tibetanus), foxes (Vulpes vulpes). Strains of spirochetes isolated from O. papillipes were used to infect the following (N. G.): long-eared hedgehog /Erinaceus auritus/, the Caspian souslik (Citellus fulvus), Siberian polecat (Putorius eversmanni), badger (Meles meles), wolf (Canis lupus), Tartar fox (Vulpes corsac), saiga (Saiga tatarica), the gray hamster (Cricetulus migratorius) and the common hamster (Cricetus cricetus). As is seen from this list, wild ungulates, many carnivores, and a number of species of rodents were found to be susceptible to the spirochetes of tick-borne relapsing fever.

This information considerably expands our ideas of the structure of the natural focus of tick-borne relapsing fever and its spread to human dwellings. Observations of the life and behaviour of mammals listed above and other desert mammals permit us to outline the distinctive means of circulation of spirochetes in nature in the north of the area of distribution of their vectors.

The biotopes of the ticks O. papillipes and O. tartakovskyi in the north of their areas of distribution, located literally next to one another, are unique places in which spirochetes are exchanged between these two species of ticks. The biotopes of O. papillipes in this combination are at the same time the "portals" of exit of spirochetes to domestic animals (the dog) and man.

The disease, tick-borne relapsing fever, in people in Kazakhstan, according to the data of the Republic Epidemiological Service, is recorded in the Southern Oblasts in the area of distribution of the tick vectors O. papillipes and O. tartakovskyi. The determination of the existence of typhus fever within the boundaries of the Republic, transmitted by ixodid ticks, is new for Kazakhstan public health. The region

of distribution of endemic typhus fever foci in the Soviet Union, which is tremendous in its extent -- from the Crimea to the Far East -- up until recent years was interrupted within the boundaries of Kazakhstan, whereas from a zoological standpoint (the existence of possible reservoirs of the infection and vectors of it) Kazakhstan should not have been an exception.

All species of rodents are represented among the fauna of Kazakhstan, reservoirs of this type of rickettsial disease, while of the vectors known only two species of ticks are absent: Dermacentor nuttalli and D. silvarum. The presence, in addition, of natural-geographic features in common between the places in which the natural foci of this rickettsial disease are located with those in Kazakhstan gave us reason to suspect the spread of this infection to KazSSR. Actually, beginning with 1949, tick-borne typhus fever began to be diagnosed in Kazakhstan. The first cases were described by our co-worker Professor Ye. N. Bartashevich in Alma-Atinskaya Oblast, where the existence of vectors was also determined -- the ticks D. marginatus and Hyalomma punctata. The pathogen Ixodoxenus sibiricus was isolated both from sick people (Bartashevich) and from ticks (Arkhangel'skiy).

Tick-borne rickettsial fever in Alma-Atinskaya Oblast has a well-expressed spring-summer seasonality (from April through July).

The zone of tick foci in nature has been determined reliably in the forest strip of Zailiyskiy Ala-Tau. In 1955, Ye. N. Bartashevich described cases of tick-borne rickettsial disease in South Kazakhstan (Pakhta-Aral), in West Kazakhstan, and even in the north of the Republic -- in Pavlodarskaya Oblast. There is no doubt of the fact that this disease has spread to Kazakhstan considerably more extensively than was hitherto known.

In West Kazakhstan, in the area of clayey wormwood-herbaceous semidesert, one of us (M. R.) found pathogens of tick-borne typhus in dwarf sousliks, Caspian sousliks, and in gamasid ticks taken from infected sousliks. This finding indicates the presence of a new, hitherto unknown structure of the natural focus, where desert animals -- sousliks -- appear in the role of donors, and their ectoparasites come out in the role of vectors -- the gamasid ticks.

Q fever is a unique acute infectious disease of people, agricultural and wild animals, the pathogen of which is Rickettsia burneti, which is widespread within the boundaries of the USSR. This disease also occurs in Kazakhstan. In the past three years our co-worker (Ye. N. Bartashevich) determined serologically the existence of this infection in almost all oblasts of the Republic.

This disease, which is of a zoonotic character, has been found by various investigators of the USSR in many species of wild animals. The pathogen of Q fever has been isolated from the bodies of ixodial, argasid, gamasid ticks and thrombiculid mites. It has been determined that these ticks and mites are responsible for the circulation of the pathogen in nature from one species of wild animals to another and pass it from wild to domestic animals. Thereby, the domestic

animals are apparently the main source of infection of man. Of particular importance are long- and short-horned cattle, although horses, asses, mules, yaks and dogs become sick with this rickettsial disease. Many domestic birds are also susceptible to Q fever: pigeons, ducks, chickens, geese, and turkeys. According to Balayin's data (1956) wild birds are not free of this infection either: sparrows, swallows, yellow buntings, chaffinches, wagtails, redstarts, woodpeckers and greenfinches.

The extensive distribution of Q fever in Kazakhstan is brought about by the fact that this infection is characterized by anthropurgic foci along with natural foci, the exchange of the pathogen between which occurs in a most intense manner because of the well developed synanthropy in the livestock-raising economies of KazSSR and the existence of extensive contact between synanthropes and exoanthropes [animals in contact with man and animals not in contact with man] and directly with agricultural animals.

The relation of anthropurgic foci to natural foci and the predominant significance of the arthropod factor are responsible for the unchanging spring-summer seasonality of the disease -- May-June (Bartashevich). In addition, in years in which there is an early and hot spring, when the census of ticks increases sharply and rodents are most active, the number of sick persons considerably increases. In such years, according to the data of Ye M. Bartashevich (1956), the morbidity rate among agricultural animals reaches imposing dimensions. Thus, in 1953-1955, in Alma-Atinskaya Oblast of KazSSR infection with R. burneti, according to serological data, amounted to the following: in long-horned cattle, 29 percent (cows in the suburbs of Alma-Ata, 40 percent) and in sheep (55 percent). Thereby it is characteristic that cows and sheep which were being driven in the desert region were infected to the extent of only five percent. The pathogen of Q fever was isolated by Bartashevich also from the blood of a patient by means of infecting a guinea pig.

Therefore, the "blank spot" on the map of tick-borne rickettsial diseases has been filled in by these observations. Kazakhstan does not represent an exception in this respect.

An essential problem in the matter of study of leptospiroses in Kazakhstan is the detection of natural foci of pathogenic leptospiras and the study of the ecological conditions of the foci as well a study of leptospirosis of agricultural animals as sources of diseases in man and as a link in the circulation chain of leptospiras in nature.

Our co-workers T. A. Krepkogorskaya and D. M. Shapiro (1954) found natural foci of leptospirosis in the South, North and West of Kazakhstan. The reservoir of leptospiras in nature (local serological types) in the South of Kazakhstan were the great sand rat [Rhombomys opimus], the crested jird (Meriones tamariscinus), alactaga (Allactaga elater), the long-eared hedgehog, the Siberian polecat, the intermediate souslik [Citellus intermedius] and the dwarf souslik [Citellus pygmaeus], and in the North of the Republic, water vole (Arvicola terrestris) and harvest mouse (Micromys minutus).

Within the boundaries of Kazakhstan this infection along with leptospirosis in people has been determined by cultural and serological methods in long-horned cattle, sheep, horses and camels. Characteristic in the structure of the natural foci of local leptospiroses is the involvement of the pathogen of desert animals not connected with water bodies by virtue of their habitats in the cycle. In connection with this, it would be fitting to report observations which should attract the attention of epidemiologists and parasitologists. Our co-worker (Krepkogorskaya) along with one of us (M. R.) isolated pathogenic leptospiras of the L. grippotyphosa type from the bodies of D. marginatus ticks. These ticks were collected in a focus endemic for leptospirosis from long-horned cattle. Work in this area is being continued.

Active accumulation of material on the study of the possibility of natural focalization of brucellosis in the Soviet Union has been going on for more than 15 years. Our investigations in Kazakhstan, begun by one of us (I. G.) in 1941 and then continued by a group of investigators of the Academy of Sciences KazSSR, permitted us to demonstrate many species of wild vertebrates and parasitic arthropods under natural conditions spontaneously infected with brucellas and to determine their susceptibility to this infection. Even at the beginning of these investigations Academician Ye. N. Pavlovskiy and one of us (I. G.) expressed the idea that in brucellosis the natural focalization, if one exists, should be of a somewhat different nature. Wild animals and their ectoparasites by virtue of their synanthropy in close contact with agricultural animals in pastures and in stables, are responsible for the biocoenotic relation of one group or another of animals susceptible to brucellosis and their ectoparasites. Conditions are created in which domestic animals sick with brucellosis can become the reservoirs of brucellosis for wild animals, and, on the other hand, wild animals can become auxillary reservoirs of brucellosis, in which under definite conditions domestic animals may be infected with the infectious principle.

While the reservoir of infection constituted by the domestic animals is under human control, the reservoir associated with wild animals exists without man's active intervention. I daresay this can be the explanation for unexpected outbreaks of brucellosis where all conditions for infection known have been excluded by epizootologists. This is how we explain also the facts of the existence of naturally infected wild vertebrates and parasitic arthropods in a region where cattle infected by brucellosis is present.

We have no doubt at all about the fact that further detailed study of the epizootology of brucellosis, directed at elucidation of the role of parasitic arthropods and wild land vertebrates as reservoirs and transmitters of brucellosis, will lead to the need for revising and clarifying the epizootological basis of this disease.

Of no less medical and veterinary interest are the findings of toxoplasmas in wild animals in Kazakhstan. D. N. Zasukhin (1936) found toxoplasmas in dwarf sousliks in West Kazakhstan; one of us (I. G.) saw toxoplasmas in the Central Asian gazelle and in intermediate sous-

lika. Toxoplasmosis -- a serious infection of people and agricultural animals with natural focalization -- has been extremely poorly studied in the Soviet Union and particularly in Kazakhstan. Here, we are only beginning to study this infectious disease.

From the data presented it is not hard to see that investigations on the natural focalization of diseases being made in Kazakhstan are reinforcing the theoretical principles to the effect that the phenomenon of "natural focalization" is characteristic not only of arthropod-borne diseases but also of diseases of a non-arthropod character, of the most heterogeneous nature.

Further investigations of the natural focalization of these diseases, particularly in areas in which virgin and waste lands are being reclaimed and in workers' settlements of industrial enterprises are acquiring great importance for Kazakhstan. The problems with which investigators of Kazakhstan are confronted are great. They can be solved only with the close collaboration of practical and scientific medical and veterinary workers, with the participation, naturally, of zoologists, microbiologists and parasitologists. We ascribe great importance to the regional coordination of efforts along these lines, which we are accomplishing within the boundaries of Kazakhstan, West Siberia, and in the Republics of Central Asia. About 20 scientific institutions are working on the solution of this extremely important problem for public health and animal husbandry.

We are sure that the close collaboration between scientific and practical institutions and groups of the plague system of institutions utilizing their experience, will assist public health organs in cleaning up the natural foci of many infectious diseases still existing on our sacred soil.

pp 552-558

Investigations of Natural Foci of Diseases in Czechoslovakia

Bogumir Rosicki

The Czechoslovakian biological public was acquainted with the teaching of Yevgeniy Nikanorovich Pavlovskiy by his co-worker Professor P. A. Petrishchev at the Sixth Congress of Microbiologists in Prague in 1950. Since that time, more Soviet literature has begun to come in to us on problems of natural focalization of various infectious diseases, and some of our parasitologists have begun to study blood-sucking insects and animals which can serve as reservoirs of the disease pathogens and to clarify the significance of the teaching of Academician Pavlovskiy under the conditions of Central Europe. The basis of natural focalization of infectious diseases in Czechoslovakia becomes most understandable when we use the zoogeographic viewpoint as a basis. The territory of Czechoslovakia lies in a region of European deciduous forests, in a zone of steppes, in the Czech-German mountain massif and in the Carpathian mountain massif. From a biogeographic viewpoint forest monocultures (spruce) and a cultivated steppe are very characteristic of it.

Czechoslovakian scientific workers get the credit for the fact that they were the first to begin to work out the teaching of natural focalization of diseases, formulated by its author for regions which have just begun to be reclaimed agriculturally, for densely populated areas which have been cultivated by man for thousands of years. It would be a serious error to think that natural foci can exist only in unreclaimed or uninhabited localities.

What are the conditions for the existence of natural foci in Central Europe? Man has intervened in the development of natural biotopes of Central Europe for thousands of years. Biotopes on which human activity has not left its mark are negligibly small. Perhaps, only the mountainous areas have remained more or less untouched. In areas which lie lower, the original biotopes -- mountains, forest, marshes, forest steppes, and steppes -- have been changed gradually under the influence of grazing and ploughing, and recently also as a result of foresting and forest cultures. Biotopes have arisen which to a greater or lesser degree have been created by human activity and characteristic of which are typical biocoenoses of the cultivated landscape, well known at the present time in our fields, meadows, forest monocultures, etc. This process can be studied by archeological data far into the past of the Central European countries. Thus, about 2000-1500 years B. C. Northern. Central and Northeastern Bohemia, Southern and Central Moravia, and Southern Slovakia were relatively densely populated by people who were occupied chiefly in agriculture. About 900 B. C., in the Danube Basin an iron-using culture appeared (Hallstadt). It may be stated with certainty that human activity has had an active influence on the development of biotopes in Central Europe in the past 3000-4000 years.

If we compare the biotopes of Central Europe with the biotopes

which so far have been little reclaimed or untouched by man, if we evaluate their developments from the viewpoint of gradual penetration of man into them, we cannot help but come to the conclusion that under the influence of man some biocoenoses have disappeared entirely; others were hardly preserved; some, on the other hand, have been enriched. This has an indubitable influence on the natural foci of infectious diseases also. According to historic data and on the basis of ecologico-parasitological analysis we may, for example, suspect the existence of natural plague foci in the lowlands of the Danube and Tisza rivers, in the Carpathians, etc. (see also V. N. Fedorov, I. I. Rogozin, B. K. Fenyuk). There is no doubt that in the historic period natural foci of tularemia occupied areas of extensive wet marshy sprouts in what was then Central Europe. Human intervention limited these foci substantially.

On the other hand, human activity, conscious or unconscious, creates favorable conditions for the existence of some other natural foci. In Central Europe the natural foci of tick-borne encephalitis belong in this group.

Man has enriched certain biotopes of Central Europe with new species of animals for purposes of hunting and trade (the wild rabbit, muskrat, pheasant, and others). The quantity of game in areas of active application of biotechnical measures (which is characteristic of our Republic as a whole) has been increased considerably by comparison with what existed under the original natural conditions. In many regions of Czechoslovakia the average numbers of hares is more than 120 per 100 hectares; the average number of roe deer, five-six per hundred hectares, of pheasants, 15-20, etc. Every year, more than one million hares, more than 40,000 roe deer, etc. are caught in Czechoslovakia. Such a situation also exists in certain areas of Germany, Poland, Hungary, etc. Thereby, we should keep in mind the fact that all this game lives chiefly in forests planted by man, which have already passed through three-five generations since the middle of the 18th Century.

In accordance with this, on certain regions of the forests mentioned in Central Bohemia, specifically in areas of active breeding of game, we have observed a quantity of Ixodes ricinus L. ticks in the wild foci of tick infestation of the order of more than 3,000 nymphs and 150 imagoes on an area of 100 square meters. Repeated collections of ticks on flags in an area of 100 square meters yield 100-200 or more nymphs and imagoes. In other places man has unconsciously created foci of very numerous blood-sucking arthropods, for example, foci of tick breeding on natural pastures, where from year to year man has given large numbers of ticks grazing cattle to feed on without suspecting it.

From these brief comments it becomes clear that in Czechoslovakia there is quite a large number of ticks and their hosts in certain areas, in which the pathogens of certain diseases with natural foci may be preserved and may circulate, chiefly those of tick-borne encephalitis. True, in other areas, where in time gone by there were I. ricinus ticks they have been completely crowded out by man, for example, using actively cultivated fields and meadows.

Investigations of recent years have shown on the territory of Czechoslovakia there are natural foci of tick-borne encephalitis, lymphocytic choriomeningitis, Western equine encephalomyelitis, tularemia, some leptospiroses, hemorrhagic nephroso-nephritis, probably brucellosis, Q fever, and some other diseases.

I shall mention briefly some of the achievements in study of the natural focalization of these diseases.

Tick-borne encephalitis is the most important disease with a natural focalization in Czechoslovakia. In 1949 Gallia and co-workers isolated the encephalitis virus from a patient, and in 1949 a virus with the same qualities was isolated from I. ricinus ticks collected in the vicinity of Beroun. In 1951, an epidemic in Eastern Slovakia (the City of Rojniava) served as the direct impetus for beginning detailed comprehensive investigations of tick-borne encephalitis. To date, the following facts have been established.

The vector of the pathogen is the tick I. ricinus, from which it has been possible to isolate the virus repeatedly. Rosicki and Gavlik believe that in Slovakia the vector of the infection is also a tick, Dermacentor marginatus, from which Libikowa and Macicka also succeeded in isolating virus (from the regions of Rojniava). Thereby, transovarian transmission of the virus was proved in this species of blood-sucking ticks.

The works of Rosicki, Gavlik, Kratchvil, Macicka, and others have given us an abundance of ecological data and have made it possible to gain a better knowledge of the natural focalization of tick-borne encephalitis in Czechoslovakia by means of study, chiefly by the serological method, of various mammals and birds living in the natural foci of encephalitis. Our experience has shown that almost the entire wooded territory of Czechoslovakia 600-800 meters above sea level must be considered a single focus of tick-borne encephalitis.

The virus of tick-borne encephalitis has been isolated from the brains of Mus musculus, Apodemus flavicollis, A. sylvaticus, Clethrionomys glareolus, Arvicola terrestris, Sorex araenus, S. alpinus (Bardocz, Libikowa). Significantly elevated virus-neutralizing antibody titers have been found by Kohlman, Gavlik, Libikowa, and others in the following mammals: Microtus arvalis, Clethrionomys glareolus, Apodemus flavicollis, A. sylvaticus, Sciurus vulgaris, Sorex araenus, S. minutus, as well as in foxes, hares, roe deer, deer, and wild boars.

The results of Kohlman and Gavlik are important; they found positive serological reactions in some birds: Picus viridis, Dryobates major, Carrulus glandarius, Carduelis spinus, Fringilla coelebs, Emberiza citrinella, Certhia familiaris, Sitta europaea, Parus major, P. coeruleus, P. ater, P. cristatus, P. atricapilla, Aegithalos caudatus, Turdus ericetorum, T. merula, Erithacus rubecula, Troglodytes troglodytes, and others.

Further, we should emphasize very interesting serological investigations by Kohlman and Gavlik in bats (Chiroptera) which have not been explained in detail. Repeatedly positive reactions were found in Bar-

Barbastella barbastellus, Myotis myotis and in Rhinolophus hipposideros.

Of the mammals and birds mentioned above in which contact with the virus of tick-borne encephalitis has been established in Czechoslovakia, of the greatest importance for preserving the virus in a natural focus are Apodemus flavicollis [yellow-necked mouse], A. sylvaticus [wood mouse] and Clethrionomys glareolus [bank vole].

I should also like to note that Rasha, Bardocz and Blaschkovicz, while investigating a large encephalitis epidemic in the City of Rojniava in 1951 in which there were more than 600 persons afflicted, expressed the idea, on the basis of a detailed epidemiological analysis, that the encephalitis virus is also transmitted by the alimentary route through raw goats' milk. Somewhat later, this idea, independently of the investigations of the Czechoslovakian scientific workers, was confirmed by the experiments of Soviet authors (Smorodintsev).

We should also note that from the viewpoint of classification Czechoslovakian virologists put all the viruses of the tick-borne encephalitides in Central Europe in the group "other tick-borne encephalatides" (spring-summer West Russian, two-wave meningoencephalitis, and others). Our scientists doubt that according to data existing at present they can be considered independent types or even species, and that the various diseases of this group can be considered nosologic entities.

On the basis of a thorough ecologico-parasitological analysis of tick infestation of certain biotopes in Central Europe, supplemented by the results of virological and epidemiological investigations, we can present a plan of classification of the Central European natural foci of tick-borne encephalitis, which are distinguished by characteristic ecologico-parasitological and other features:

1. Natural foci in the lowland and hilly forest regions (up to 600-800 meters above seas level). They coincide with places of active tick infestation, for the most part in mixed or deciduous forests (in isolated cases, also in coniferous forests), in which cattle do not graze at the present time. Now, in these foci of tick infestation the main source of blood for the Ixodes ricinus imago are wild animals which, as I mentioned above, are intentionally bred by man. Transmission of the virus to man by ticks is accomplished when he walks or works in the woods. The Beroun basin can serve as an example. This Central European type of forest foci of encephalitis in the Central European forests is different from the natural foci of encephalitis in the virgin taiga, which has not been reclaimed so far by man. Central European "wild foci of tick infestation" are associated with forest which has been subjected to the influence of man repeatedly in the past (conversion of forest to field and, conversely, active grazing of cows, hogs, goats, planting of forests in certain places for the third or fourth time now!). The grazing of cattle in forests, which was stopped in Bohemia and Moravia only in 1750-1850, causes us, apparently, to place this type of focus alongside the pasture foci of tick infestation. Under the influence of man and contact with his activities these foci have undergone a thousand years of development since the original natural foci in the virgin for-

est, but even at the present time they are always associated with the presence of wild animals as feeders of tick images in Central Europe.

2. Natural foci associated with place of accumulation of ticks in pastures in those places where the cattle graze on uncultivated lands covered with abundant brush. Such foci are distributed chiefly on the pastures of Slovakia approximately up to a level of 600-800 meters above sea level. The main source of blood for the imago here is the grazing cattle. Judging by data so far in existence, very favorable conditions for the existence of such foci exist on limestone soils, where the characteristics of the vegetation have probably for a long time created pasture conditions. In foci where ticks accumulate in pastures epidemics of encephalitis are known, associated chiefly with the consumption of raw goats' milk. Rojniava can serve as an example.

3. The natural foci of encephalitis of the mixed type located in regions where pastures with an abundance of ticks border directly on tick-infested forests and where an exchange of hosts occurs at the imago stage (game, cows, goats). This type is transitional and mixed both from the ecologico-parasitological and from the epidemiological standpoints. Foci in certain places of Southern Bohemia and Southern Slovakia can serve as examples.

4. Natural foci associated with hilly or mountainous regions, almost without ixodial ticks. At a height of about 1000 meters above sea level the distribution of the I. ricinus tick stops. The natural focus of this type was found by Czechoslovakian investigators last year (Bardocz and others). The virus of tick-borne encephalitis was isolated from the brains of Arvicola terrestris [water vole], Sorex alpinus [shrew] Apodemus flavicollis and Mus musculus [house mouse] (in a house) in the Tatra Mountains (about 1000 meters above sea level). It may be supposed that the transmission of the virus to man occurs here only exceptionally and that the virus circulates among small mammals and is probably transmitted by ticks of the subfamily Gamasoidea or by other arthropods. The existence of these foci of encephalitis has been incompletely studied to date, but, according to the data of Docent Gringsla, foci of encephalitis exist at these altitudes in the Alps.

Under the conditions of Central Europe, where it is impossible to cut down any more trees or break the tradition of breeding agriculturally important animals, it is important to seek out special means of prophylaxis of tick-borne encephalitis. This applies chiefly to foci of the first and third types. Unfortunately, these methods have as yet been very poorly studied for the conditions of Central Europe. The matter is clearer with regard to the pasture foci of tick-infestation.

The existence of natural foci encephalitis in Central Europe is not only an interesting example, but it obliges us to do further work. In the areas reclaimed by man in the original foci natural foci modified by man can occur, the potential of which can be increased further by comparison with the original as a result of the unintentional activity of man.

Equine encephalomyelitis of the Western equine encephalomyelitis

type. The pathogen of this disease was isolated by Libikova in 1953 during operations of a comprehensive expedition to Eastern Slovakia: it was isolated from Ixodes ricinus ticks, from Clethrionomys glareolus voles and Sorex araneus shrews [the common shrew]. In 1954, during comprehensive work along the Danube, Bardoes isolated this virus also from Apodemus flavicollis. Danes (1956) isolated the virus of equine encephalomyelitis from the brain of a dead man.

Unexpected detection of this virus from natural foci without preliminary epidemiological indications confronts us with the problem of studying its significance for domestic animals and, as the observation of Danes shows, for man.

Lymphocytic choriomeningitis. Strains of the pathogen of lymphocytic choriomeningitis have been isolated repeatedly from Mus musculus, Apodemus flavicollis, A. microtus [harvest mouse] in Bohemia and Slovakia, frequently from rodents living in wild nature (Benda, Bardocz, Libikova and others).

Q fever. The group at the Institute of Epidemiology and Microbiology (Pach , Syrucek, Gavlik and others) made a systematic investigation of the distribution of Q fever in Western Bohemia. Detailed investigations by this group showed that Q fever in this area is of the nature of anthropozoonosis, which is spread among domestic animals, which are the sources of infection of man. In this phase of the epidemic and epizootic processes the vectors play only a secondary role. The natural foci of Q fever are developing in the Czechoslovakian Republic, as the works of our investigators have shown, in a direction opposite to the usual for diseases with natural foci. The infection is gradually spreading from domestic animals to wild nature, as a result of which natural foci of Q fever are occurring in certain areas of Czechoslovakia.

In the Czechoslovakian Republic strains of Coxiella burneti have been isolated from Ixodes ricinus (Benda, Ren), from Dermacentor marginatus, Haemaphysalis punctata (Nijnanski and others), from Ornithomyia biloba (Syrucek and Gavlik).

In wild animals and birds, it has been shown serologically that many of them, living in the vicinity of sick agricultural animals, have been in contact with the pathogen of Q fever. Gavlik, Syrucek and others found postive results in the following species of birds: Dryobates major, Chloris chloris, Emberiza citrinella, Tringilla coelebs, Motacilla alba, Phoenicurus ochruros, Hirundo rustica, Delichon urbica, Passer domesticus, and in the group of mammals, in Rattus norvegicus [brown rat]. Serologically, Q fever was also found in Mus musculus, Sorex araneus, roe deer and deer (the works of Brezina).

The means of occurrence of natural focalization of Q fever need further study. According to the data of some other investigators (Ren Radman) it may also be supposed that in various places of our territory non-imported natural foci of Q fever may exist.

Tularemia. In a natural focus of tularemia in South Moravia Taiberger and Benda (VMA) isolated strains of Bacterium tularense from Ixodes ricinus and Dermacentor pictus ticks and from Clethrionomys glar-

colus and Apodemus flavicollis rodents, while Aldova isolated them from muskrats in Western Bohemia.

Leptospirosis. Important data have been obtained in the investigations of natural foci of leptospirosis. This problem has been worked out thoroughly by Kmety, Pokorni and others. In the Czechoslovakian Republic at the present time 18 different species of animals are known -- the reservoirs of leptospiras in wild nature belonging to 10 species and types.

To date, little attention has been given to the possibility of existence of natural focalization of some infections of domestic animals, such as brucellosis, ornithosis, rabies, toxoplasmosis, etc. It may be supposed that in Czechoslovakia extensive sources of brucellosis exist in nature (Mijnanski). Krjivnika and others isolated more than 70 strains of Brucella suis from hares.

Extensive microbiological, chiefly virological and leptospirological investigations could not have been accomplished to such a degree if bacteriology and parasitology were not fully developed. In the study of diseases frequently it has been parasitology which has indicated the way along which the investigation of various aspects of a natural focus proceeded. Parasitologists have noted the most important links of the focus, have determined the interrelationships between various constituents of the biocoenosis of the focus, have classified the biotope, and have generally been guided by the ideas of Academician Ye. N. Pavlovskiy on matters of parasitological investigation of natural foci of infectious diseases.

Czech and Slovak investigators of natural foci of infectious diseases are developing the teaching of Academician Pavlovskiy as applied to the conditions of a locality which has been cultivated for a long time. On the model of Soviet science, using comprehensive collaboration by clinicians and epidemiologists, microbiologists, parasitologists, zoologists and other specialists, they have found a suitable method of solving large-scale and complex problems in a short time (two-three years), the solution of which is beyond the capacities of a single investigator.

The prospects and final aim of investigations of natural focalization are to preserve the health of the workers of Czechoslovakia, to protect animal husbandry and plant growing from losses inflicted by contagious diseases with a natural focalization, and to concern ourselves with the elimination or disinfection of the foci. From these viewpoints the investigations have hardly been begun and require further development.

The results achieved oblige scientific workers in all the disciplines included in the investigation to develop further work for the protection of health and the agricultural efforts of Czechoslovakian workers and for the enrichment of science with new data in even closer brotherly collaboration between Czechoslovakian and Soviet scientific workers.

PP 559-563

Investigations of the Natural Reservoirs of Anthropozoonoses in Poland

Information Bulletin

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We began our work on the study of anthropozoonoses in 1944, but at that time these works dealt only with anthropurgic biotopes and agricultural animals. Beginning with 1950 we have started to occupy ourselves with the natural landscapes and biocoenoses of small mammals.

Before presenting the study of anthropozoonoses, we consider it necessary to make one terminological comment. In classifying infectious diseases we distinguish between three terms: "zoonoses", that is, infectious diseases of animals alone, for example, hog plague, long-horned cattle plague; "anthroponoses", infectious diseases of man alone (typhoid and typhus fevers), including those which are transmitted by means of vectors, for example, lice; "anthropozoonoses", that is, infectious disease of animals which are transmitted to man either directly or through vectors.

This terminology has been accepted by the Commission of Scientific Council of the Ministry of Health of Poland for the purpose of classifying the particularly dangerous infectious diseases, among which the Commission included plague, smallpox, tularemia, encephalitides with natural focalization, anthrax, glanders, psittacosis, trichinelliasis, and leptospirosis.

Polish landscapes are very heterogeneous, beginning with the territories of mountains and hills (Carpathians, Tatras) to the lowland, marshy and forest plains (Belovejski and other dense forests, the strips of territory above the Vistula, Bug, Oder) and biotopes lying on the shore of the Baltic Sea and in the deltas of the Vistula and Oder.

The territory of Poland, unfortunately, has repeatedly been the pathway and the theatre of military operations, which may have and has had a serious reflection on the epidemiological situation in the country today.

Of particular importance is the boundary of the biotopes of the Soviet Union (ecological characteristics of Kaliningradskaya Oblast, Soviet Belovezhskaya Pushcha, and Poles'ye, the territory and forests of Volynya and the Carpathians), the biotopes of Germany, lying behind the Oder and the Niesse Rivers, and the biotopes of Czechoslovakia.

As a result of the war, in 1945-46, a colossal multiplication of mouse-like rodents occurred in Poland, particularly in the Western regions and in the Southeast of Lyublinskaya Oblast. The multiplication

was so great that the rural population in places liquidated their farms and left the lands infested with rodents.

The government at that time placed me at the head of a commission for the investigation of this catastrophic multiplication of rodents on fields and in houses of rural areas, for the study of the causes of this phenomenon, of the species composition of the rodent population, of the developmental dynamics and migration of rodents, microbiology and epizootology. At that time, the main species involved was the common vole, Microtus arvalis, while the causes of the epizootics among the mouse-like rodents were Pasteurella multocida and Salmonella. Pasteurella tularensis was not found.

For the purpose of rapid extermination of mouse-like rodents in the houses and in the fields we used chemical and bacteriological agents. After becoming acquainted with materials on the extermination of rodents in Copenhagen and in Paris we decided to use the Salmonella danyszi* strain from the Pasteur Institute for bacteriological control of rodents. In 1945-1946 about 50,000 liters of this culture were used as baits. No complications were recorded among people or domestic animals, and the effect on some territories was good.

Further investigations were made in Shchetsinskaya Oblast, where tularemia was found in people and in hares. In the biotopes where tularemia was found small mammals were caught by means of cylinders dug into the ground.

In 1953 17 species had been detected with the following number of specimens: 1. Microtus arvalis, 2607 specimens; 2. Microtus ratticeps, 162; 3. Microtus agrestis, 1; 4. Pitymys subterraneus, 1; 5. Arvicola terrestris, 2; 6. Mus musculus, 84; 7. Mus polonicus, 6; 8. Micromys minutus, 14; 9. Epimys norvegicus (Rattus norvegicus), 21; 10. Apodemus agrarius, 49; 11. Apodemus sylvaticus, 19; 12. Sciurus vulgaris, 8; 13. Sorex araneus, 148; 14. Sorex minutus, 97; 15. Talpa europea, 22; 16. Neomys fodiens, 5; 17. Erinaceus roumanicus, 1.

In striving to obtain a scientifically substantiated picture of the location of the small mammals in various biotopes of Poland we made further investigations of the rodent fauna, in Lyublinskaya Oblast along the Rivers Bug and Solokia, where swamp fever in people is endemic. Here, the same cylinder method was used for catching small mammals in 1955-1956. Characteristic of the landscape of this locality is a junction between dry fields and marshes, wet meadows and peat bogs. Simultaneously with catching small animals we made methodical meteorological observations in order to clarify the effect of climatic factors on the multiplication of small mammals. Ten parameters were studied: barometric pressure, air temperature (by dry and wet thermometers); water vapor pressure, relative humidity, the temperature of the surface portion of the soil, the direction and velocity of the wind, characteristics of clouds and insolation.

There were marked differences in the climatic conditions between 1955 and 1956. The summer of 1955 was humid and warm; the summer of 1956, conversely, was drier and colder. However, we did not find any

*[the Danysz variety of S. enteritidis]

definite differences in the lives of the rodents.

As a result of catching small mammals from July through September 1955 in the environs of the village of Nemiruvek with the junctions of biotopes characteristic of them, 918 mammals of 14 species were caught, namely: 1. Microtus arvalis, 448 specimens; 2. Mus musculus, 157 specimens; 3. Arvicola terrestris, 75; 4. Ondatra zibethica, 60; 5. Epimys norvegicus, 43; 6. Apodemus sylvaticus, 30; 7. Erinaceus roumanicus [hedgehog], 23; 8. Neomys fodiens [water shrew], 22; 9. Sorex araneus, 27; 10. Cricetus cricetus, 10; 11. Apodemus agrarius [field mouse], 8; 12. Micromys minutus [harvest mouse], 8; 13. Talpa europea [mole], 3; 14. Crocidura leucodon [white-toothed shrew], 2.

In the same locality in 1956 a total of 929 rodents of the following 17 species were caught: 1. Microtus arvalis, 360 specimens; 2. Mus musculus, 165; 3. Microtus ratticeps, 135; 4. Arvicola terrestris, 116; 5. Erinaceus europaeus, 10; 6. Ondatra zibethica, 27; 7. Apodemus agrarius, 1; 8. Crocidura leucodon, 3; 9. Talpa europea, 3; 10. Sorex minutus, 18; 11. Neomys fodiens, 23; 12. Cricetus cricetus, 33; 13. Mustela mustela, ; 14. Micromys minutus, 3; 15. Clethrionomys glareolus, 10; 16. Epimys norvegicus, 7; 17. Sorex araneus, 1.

As a result of the expeditionary investigations made in Belovezhskaya Pushcha in 1955 and 1956 22 species of mammals were caught. The main species here were Clethrionomys glareolus and Apodemus flavicollis. Third place with regard to the census was occupied by Sorex araneus. Of the group of new species which were not found in the other biotopes, mention should be made of Dryomys nitedula [dormouse] and Sorex macropygmaeus.

Note should also be made of the many years of methodical work of the Institute of Zoology of Lublin University on the study of the location of sousliks in Lyublinskoye Voyevodstvo [province]. Settlements of sousliks in Lyublinskoye Oblast were connected historically with their settlements in Volynskaya and L'vovskaya oblasts. This work is of great sanitation significance, and we shall continue it methodically.

With the aid of the Main Sanitary-Epidemiological Administration of the Ministry of Health and the Polish Academy of Sciences our institutes, particularly the Institute of Naval Medicine in Danzig and the Institute of Rural Hygiene in Lublin are continuing work in making out the first zooecological map of distribution of small mammals and their ectoparasites in Poland, using an example from Soviet medical zooecological and epidemiological investigations in this connection.

All of the mammals listed above were carefully studied by the methods of bacteriology, virology, serology, histopathology and others. An investigation was also made of many other wild animals, including birds. Of the mammals mention should be made of Lepus europaeus [rabbit], Oryctolagus cuniculus [rabbit], Mustela nivalis [weasel], Martes foina [marten], as well as certain forest ruminants. Of the birds mention should be made of Corvus cornix [raven], Buteo buteo [hawk], Tyto alba, Strix aluco [owl], Fulica atra [coot], Pica pica [magpie], Pluvialis agrarius [plover], Cuculus canorus [cuckoo], Hir-

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undo rustica [swallow].

In the investigation of wild animals the following pathogens of anthropozoonoses were found: 1. Pasteurella tularense -- in common voles, Ixodes ricinus ticks and hares. 2. Pasteurella multocida-- frequently in mouse-like rodents and hares. 3. Pasteurella rodentium -- frequently in mouse-like rodents and hares. 4. Brucella brucei -- in hares. 5. Listerella monocytogenes -- in common voles and hares. 6. Erysipelothrix -- in the wild pig and certain wild ruminants. 7. Leptospira grippotyphosa, L. sejro, in all small mammals. 8. Salmonella typhi murium, in mouse-like rodents. 9. Salmonella typhi abdominalis, in rats. 10. Mycobacterium tuberculosis, bovine type -- in common voles. 11. Leptospira icterohaemorrhagiae -- in rats. 12. Rickettsias -- in rats. 13. Virus of tick-borne encephalitis -- in mouse-like rodents, ticks and mosquitoes. 14. Trichinella spiralis -- in mouse-like rodents.

During the epizootics among sousliks in Lyublinskoye Voyevodstvo we found Pasteurella multocida and P. rodentium. In domestic animals Coxiella burneti, B.anthracis and others were found.

Investigations are being made on toxoplasmas in rodents.

I have presented briefly the basic results of many works which were done even before the war by Anigstein, Weigl, Zvej, Parnas and in the People's Democracy of Poland, by Skrodski, Mojicki, Parnas, Tvorek, Penel, Zvej, Sirm, Psesmicki, Dombrowski, Linkmajerova, Javecki, Hodkowcki, Kozar and other scientific workers of sanitary-epidemiological institutions.

In conclusion, as a member of the scientific council of Ministry of Health of Poland as well as in the capacity of a former worker in the World Health Organization of the United Nations (Geneva) and a former member of the International Bureau on Epizootics (Paris), I consider it necessary to evaluate the achievements in Poland critically and to advance certain important general concepts at this great conference of Soviet scientists and specialists.

Polish scientists, undoubtedly, have made a great step forward along the line of investigating the fauna of certain landscapes of Poland from a medical standpoint and ecology of a number of animals. This has become possible, because, first of all, the government has given us the necessary conditions, organizing our institutes; secondly, the ideas of preserving the health of the rural population have obtained complete recognition and support; thirdly, Polish science has established contact with world science and Soviet medical science. Note should be made of the significance of the teaching of Academician Ye. N. Pavlovskiy, of your [this Polish writer is addressing a Soviet group] literature, of contact with your scientists, who were guests and conferees in Poland and whom we have recognized here. However, on becoming acquainted with your achievements, particularly at this conference, we see that we have far from enough cadres of medical zoologists, ecologists, parasitologists, and other specialists. We shall have to correct this deficiency soon.

We must organize even better collaboration, international sym-

posia, exchange of publications, scientists, etc. We must take an active part in the work of the World Health Organization of the United Nations. The problems which we are studying require collaboration on a world-wide scale, despite the difficulties standing in the way of this. Thereby, we must be guided primarily by the idea of welfare and health of the population in all countries of the world, by the sacred idea of peace throughout the world!

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1233